



1803 BUILDING 14 December 2004 The Dow Chemical Company Midland, Michigan 48667

Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
Attention: Chemical Right-to-Know Program

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Dear Sir or Madam,

Please find enclosed a disk containing robust summaries and a proposed test plan for the following intermediate production stream:

CAS# 63890-96-5 Chlorinated C3 Stream

The information is being submitted for the HPV Challenge Program, AR-201, on behalf of The Dow Chemical Company, and the files are provided in Microsoft® Word format.

Should you need further information regarding the submission, please contact me at any time. You may also address comments or concerns to Dr. William Stott of The Dow Chemical Company at (989)-636-8203.

Kind Regards,

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201-15745A

HPV Challenge Program

TEST PLAN

For

C3 Chlorinated Hydrocarbon Stream (CASRN 63890-96-5)

CASRN:

63890-96-5

Sponsor

The Dow Chemical Company

Midland, Michigan

Date of Submission:

14 December 2004

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10 December 2004

Test Plan for C3 Chlorinated Hydrocarbon Stream

(CASRN 63890-96-5)

I. SURROGATE JUSTIFICATION

CAS 63890-96-5 C3 Chlorinated Hydrocarbon Stream consists of several chlorinated 3-carbon chemicals which are produced as intermediate streams from several manufacturing product lines. Though somewhat variable, the largest volume components of CAS 63890-96-5 are 1,2-Dichloropropane (approximately 65%), Trichloropropene (8%), and 2-Chloropropene (6.5%) The remaining CAS 63890-96-5 C3 Chlorinated Hydrocarbon Stream is composed of a number of chlorinated propenes with no other single component present at more than a 5% of the total stream.

PDC will be used as a "surrogate" chemical for defining the toxicity of CAS 63890-96-5 C3 Chlorinated Hydrocarbon Stream as part of the HPV program based upon its high volume percent of the stream and the wealth of mammalian and environmental toxicity. PDC (65%), Trichloropropene (8%) and 2-Chloropropene (6.5%) all exhibit remarkably similar toxicity profiles (Bingham, 2001). While the acute oral and dermal LC₅₀'s of Trichloropropene and 2-Chloropropene are lower than those of PDC, toxicity via inhalation is very similar. The three components show very comparable subchronic NOAEL's, are all considered to be non-carcinogenic in *in vivo* testing, and all three have mixed or positive mutagenicity findings. They are similarly all considered to be non-teratogenic, although there were findings of mild delays in ossification in the fetuses at comparable dose levels. Based on the consistent toxicological profiles of the three compounds most abundant in the stream, it is reasonable to identify PDC as the surrogate for the stream.

Significantly, PDC has also been evaluated previously as part of the OECD SIDS program (http://www.oecd.org). It was judged to be "of low priority for further work" at SIAM 17 (November 2003) indicating the adequacy of its database for coverage of OECD SIDS endpoints. Information presented in the present HPV Test Plan and related IUCLID Robust Study Summaries were drawn heavily from the complimentary OECD SIDS documentation.

II IDENTITY

A. Identification of the Substance

CAS Number: 78-87-5

IUPAC Name: 1,2-Dichloropropane

Molecular Formula: C3H6Cl2 Molecular Weight: 201.91

Synonyms: PDC, Propylene Dichloride

The compound is a colorless liquid in the pure or neat state. Because of its structure, PDC has a high vapor pressure, and high partition coefficient (log K_{ow}). MacKay Level III fugacity modelling predicts that the substance will partition predominately to air.

B. Purity/Impurities/Additives

The compound is sold in its pure form.

C. Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Physical state	colorless liquid
Melting point	-70 °C
Boiling point	95-96 ° C
Vapour pressure	66.2 hPa at 20° C
Water solubility	2800 mg/m ³ at 25° C
Partition coefficient n- octanol/water (log value)	2.0

III DEVELOPMENT OF ROBUST SUMMARIES AND STUDY SCORING CRITERIA

The Dow Chemical Company has chosen to use the IUCLID (International Uniform Chemical Information Database) format for preparation of robust summaries for the HPV program. Because many of the fields in the IUCLID database program are outside the scope of the HPV program, these fields are typically left blank in the IUCLID robust summary. Scoring of studies from company files or from the literature for reliability to fulfill the testing requirement for each endpoint used a system similar to that published by Klimisch *et al.* (1997). Studies were given a score of "1" if the data could be considered valid without restriction based on the completeness of the protocol and adequate details in reporting. Studies were given a score of "2" if the data and study design could be considered scientifically valid to address the endpoint but with restrictions due to lack of various technical or reporting details or deviations from current OECD guidelines. Studies were given a score of "3" if their conduct was not acceptable and "4" if there wasn't enough information present to assign a reliability rating. However, a

study receiving a score of "4" could provide supplementary information that could be used to address the endpoint in a weight of evidence evaluation in the absence of other data.

IV TEST ENDPOINT RESULTS

Evaluation of the data for PDC leads to the conclusion that the quantity of data to adequately represent the toxicological and ecological profile of CAS 63890-96-5 C3 Chlorinated Hydrocarbon Stream. A summary of the data on each of the HPV/SIDS endpoints for the compound follows.

A. Physical Chemistry

Melting Point

IUCLID 2.1: PDC is a liquid in the neat or pure state with a melting point of –100.4°C (Mackay, 1993). The melting point is well-documented in peer-reviewed literature and databases. **No additional testing is required.**

Boiling Point

IUCLID 2.2: The boiling point for PDC is well-documented (Mackay, 1993).No additional testing is required.

Vapor Pressure

IUCLID 2.4: The vapor pressure for PDC has been well-documented in published literature and chemical handbooks. The experimental value is 66.2 hPa at 25°C (Mackay, 1993). **No additional testing is required.**

Partition Coefficient

IUCLID 2.5: Partition coefficient is well-documented (Mackay, 1993) for PDC. No additional testing is required.

Water Solubility

IUCLID 2.6.1: Measured data indicates that PDC is soluble in water. Measured aqueous solubilities of 2800 mg/m³ is reported. (Mackay, 1993) The low log K_{ow} also supports the reported data for water solubility. Sufficient data exist for this endpoint to characterize water solubility for the compounds. No additional testing is required.

B. Environmental Fate

Photodegradation

IUCLID 3.1.1: The compound does not absorb light >290 nm, and therefore direct photolysis is not possible (Howard, 1990). Vapour phase photolysis under simulated sunlight did not occur after prolonged exposure (period not stated). Experimental determination of its rate of reaction with hydroxyl radicals gave a half-life of >23 days. A computer estimate of its half-life due to H-atom abstraction by hydroxyl radical yields a calculated half-life of 7.12 days. No additional testing is required.

Stability in Water (Hydrolysis)

IUCLID 3.1.2: PDC does not possess a molecular structure that contains functional groups subject to rapid hydrolysis under neutral ambient conditions; the 16 fe at pH 7 is estimated to be 15. 8 years (Mackay, 1993).

Hydrolysis produces 1-Chlor-2-propanol and HCl. This testing endpoint is well characterized. **No additional testing is required.**

Environmental Transport

IUCLID 3.3.1: Based upon the EPIWIN Level III Fugacity Model, PDC is expected to stay primarily in air, as is shown in the following table. The assumption is for emissions to air only (according to U.S. EPA TRI Database, >99.9% of reported PDC emissions are to the atmosphere).

Predicted Environmental Partitioning of PDC

Compartment	Level I	Level III
Air	98.02	98.85
Water	1.82	0.93
Soil	0.16	0.21
Biota	<0.01	ND
Sediment	ND	<0.01

The EPIWIN Level I Fugacity Model results predict a similar fate. Advection in air accounts for 88.6%, and reaction in air for 11.2%, of the removal rate. Advection and reaction in water, sediment, and soil account for 0.2% of removal rate. Although the values obtained using this model should not be regarded as quantitative, the model results are consistent with the properties of the compound. **No additional testing is required.**

Biodegradation

IUCLID 3.5: Biodegradation is the conversion of a chemical by microorganisms in the environment into its simpler components and ultimately to carbon dioxide and its other constituent molecules. Chemicals are classified as readily biodegradable by the Organization for Economic Development (OECD) guidelines if there is a 70% degradation of dissolved organic carbon within a 10-day period during a typical 28-day laboratory protocol.

No biodegradation of PDC was detected when PDC (150 mg/l) was incubated aerobically with municipal activated sludge (1,000 mg/l mixed liquor suspended solids) for 28 days in an OECD 302B (modified EMPA Zahn-Wellens test), conducted according to GLP requirements (2002). However, there are published examples of acclimated municipal and other systems where PDC does undergo biodegradation, including addition of cofactors (acetate and methanol), and enrichment of cultures (Hauck and Hegemann, 1999; Hardy *et al.*, 1999). It is unknown if such conditions exist and if biodegradation occurs in the environment. A hydrolysis constant of 5.0 x 10⁻⁶ per hours (pH 7-9, 25° C) with a calculated half-life of 15.8 yr has been derived for water (MacKay *et al.*, 1993). These data indicate that there is sufficient information on the biodegradation potential of PDC. **No** additional testing is required.

C. Ecotoxicity

Toxicity to Fish

Walbridge *et al.* (1983) and Benoit *et al.* (1982) that demonstrate that PDC is of low acute toxicity towards freshwater fish (LC₅₀ ~140 mg/l). Although these studies pre-date current testing guidelines, they included analytical confirmation of achieved exposure concentrations which increases confidence in the reliability of the results obtained. In addition to the above, chronic aquatic toxicity data are available from a fish early life-stage (ELS). In the ELS test, a chronic NOEC of 6 mg/l was obtained for growth, and a chronic NOEC of 11 mg/l for survival, when *Pimephales promelas* was exposed to PDC for 28 days under flow-though conditions (Benoit *et al.*, 1982). The study included analytical verification of exposure concentration. **No additional testing is required.**

Aquatic Invertebrates

IUCLID 4.2: In a modern GLP-compliant guideline study using flow-through conditions and analytical confirmation of achieved concentration, Boeri (1988) obtained a 48 hr EC₅₀ of 55.9 mg/l for immobilization of *Daphnia magna*. The chronic invertebrate test, involving *Daphnia magna* (Boeri, 1988), was a GLPanalytical guideline confirmation compliant investigation with of exposure concentration. This returned a 21 day NOEC for effects on reproduction of 8.3 mg/l. Results from a 28 day study using the marine invertebrate Mysidopsis bahia (Ward et al., 1989) gave a chronic NOEC of 4.1 mg/l for effects on mortality, reproduction and growth. The study was a GLP-compliant guideline investigation peformed under flow-through conditions, with analytical

confirmation of achieved exposure concentration. No additional testing is required.

Aquatic Plants

IUCLID 4.3: Information on the acute toxicity of 1,2-dichloropropane on the salt-water algae Skeletonema costatum is available from Hughes (1988). This is a modern, GLP-compliant static guideline test, however GC analysis revealed variable losses of test substance from the screw-capped test vessels over the course of the study. As a result, no direct calculation of the EC₅₀ was possible. In recognition of this, Woodburn (2002a) used a time-weighted average AUC method (based on the measured dissipation rate of PDC from the test vessels) to calculate the no-effect concentration for this algal species. A NOEC_{120 hr} of 7.4 mg/l was thus obtained. In addition, Woodburn (2002b) calculated the percentage biomass inhibition and inhibition of growth rate over 72 hr based upon timeweighted average exposure concentration, and derived EC₅₀ values of 16.3 mg/l and 14.7 mg/l, respectively. De Groot (2002) also re-analyzed the original data from Hughes (1988) using linear interpolation after log transformation of the results obtained over the first 3 days of the study. This approach returned 72-hr EC_{50} values of 15.1 and 15.8 mg/l for biomass and growth inhibition, respectively, and a 72-hr NOEC of 8.9 mg/l. Overall the data obtained by reanalysis of Hughes (1988) supports a 120-hr algal NOEC in the range 7.4-8.9 mg/l, with 72-hr EC_{50} values of 15.1-16.3 mg/l for biomass inhibition and 14.7-15.8 mg/l for growth inhibition. No additional testing is required.

D. Toxicological Data

Acute Oral, Inhalation, and Dermal Toxicity

IUCLID 5.1.1-5.1.3 A number of studies are available which describe the acute toxicity of 1,2-dichloropropane in animals (summarized in the following table). Although pre-dating modern guidelines and GLP, the results indicate that PDC is of relatively low inherent toxicity in animals after ingestion, skin contact, or inhalation. Given the high vapor pressure of 1,2-dichloropropane, inhalation exposure appears the most relevant route while rapid evaporation from skin would be expected to minimize any potential for local or systemic effects following dermal contact.

Summary of acute toxicity data for 1,2-dichloropropane

Endpoint	Species (details)	Result	Reference
Oral	Rat (Wistar)	2200 mg/kg bw	Smyth et al., 1962; 1969
Inhalation	Rat (4 hr)	2000 ppm	Carpenter et al., 1949;
LC ₅₀		9.4 mg/l	Smyth <i>et al.</i> , 1962
	Rat (7 hr)	> 2200 ppm	Highman and Heppel,
		> 10.3 mg/l	1946
	Guinea pig (7 hr)	> 2200 ppm	Highman and Heppel,
		> 10.3 mg/l	1946
Dermal LD ₅₀	Rabbit (occluded, 24 hr)	10,100 mg/kg bw	Smyth et al., 1962; 1969

In contrast to the acute animal data, human case-reports suggest that the liver and red blood cells may be adversely affected following over-exposure by ingestion (Larcan *et al.*, 1977; Thorel *et al.*, 1986; Di Nucci *et al.*, 1988; Lucantoni *et al.*, 1992), inhalation (Pozzi *et al.*, 1985) or after prolonged, combined dermal and inhalative exposure (Fiaccadori *et al.*, 2003). Although quantitative exposure information is missing from many of these studies, and exposure to PDC is inferred rather than supported by analysis of the products involved, liver damage (hepatocellular necrosis, fibrosis, hypertension), increased serum transaminases,

haemolytic anaemia and intravascular coagulation were present reportedly in the subjects to varying extents. In two instances the subjects died after apparently ingesting 50-180 ml of industrial cleaning products (Larcan *et al.*, 1977; Di Nucci *et al.*, 1988) however the doses received by the remaining cases is not known. As a result of these findings, PDC is considered harmful by ingestion or inhalation.

No additional testing is required.

Irritation and Sensitization

IUCLID 5.2.1-5.3: Results from a GLP guideline skin irritation study (minimal redness and slight oedema), indicate that PDC is slightly irritating to skin (BASF, 1982). An early eye irritation study (BASF, 1965) reported marked redness, oedema and slight opacity 24 hr after instillation of 0.05 ml PDC into the conjuctival sac of a single rabbit. These effects were fully reversed after 8 days (no interim results available), and indicate that PDC is irritating to the eye. Case reports provide equivocal evidence that PCD may cause allergic skin conditions after uncontrolled exposure in individuals with pre-existing dermatitis. In one study, 10 workers exposed to industrial preparations containing 10-40% PDC under conditions of poor occupational hygiene (hand cleaning using these products) exhibited an allergic response after patch testing with PDC with a threshold level of 2% (Baruffini et al., 1989). However, all subjects suffered from pre-existing irritant skin-lesion and hand dermatitis that quickly resolved after cessation of exposure. In another brief report (Grzywa and Rudzki, 1981), two female workers with recurrent dermatitis responded to patch testing with 1% PDC as well as other substances present in the workplace. In contrast, results from an OECD 429 guideline mouse local lymph node assay (Woolhiser et al., 2003) found no stimulation of lymphocyte proliferation in auricular lymph nodes

from mice treated with up to 80% PDC demonstrating that it was not a sensitiser under the conditions of this test. This lack of allergic potential in the mouse is consistent with structural considerations which provide no evidence of chemical alerts (reactive groups) that would indicate a potential to act as a sensitizer. In conclusion, based on the available data, PDC is considered to provide only equivocal evidence of an ability to cause skin allergy. **No additional testing is required.**

Repeated-Dose Toxicity

IUCLID 5.4: The oral repeat dose toxicity of PDC has been investigated extensively by NTP (1986) in a series of GLP-compliant studies using male and female F344 rats and B6C3F1 mice. Key aspects of the design of these studies, along with the main findings, are summarized in the following table. The results indicate that the liver is a target organ after gavage administration, with a chronic NOAEL of 125 mg/kg bw/day in female rats (males unaffected) and a chronic LOAEL of 125 mg/kg bw/day in male mice (females unaffected). Acanthosis of the stomach (indicative of persistent local irritation) was noted in mice (rats unaffected) with a chronic NOEL of 125 mg/kg bw/d in males and a chronic LOEL of 125 mg/kg bw/d in females. Body weight was decreased 14-24% in rats (chronic NOEL_{males} = 62 mg/kg bw/d, chronic NOEL_{females} = 125 mg/kg bw/d) whereas mice were unaffected (chronic NOEL = 250 mg/kg bw/d, both sexes). The overall NOAEL values following chronic administration of PDC were 62 and 125 m/kg bw/d for male and female rats respectively. No NOAEL was derived for mice of either sex, so the LOAEL was 125 m/kg bw/d. The neurological consequences of repeated oral exposure to PDC have been

investigated in F344 rats (n = 15/sex/group) given 0 (corn oil), 20, 65 or 200

mg/kg bw/day for 13 weeks by gavage (Johnson and Gorzinski, 1988). The study followed U.S. E.P.A. guidelines and was conducted to the standards of GLP. Prior to treatment, and at monthly intervals during the study, all animals were assessed for a number of endpoints including functional observational battery, hindlimb grip strength, and motor activity. After a 13-week treatment, 4 rats/sex/dose were randomly selected for terminal examination (including histopathological examination of brain, spinal cord and nerve) while the remainder were retained (no further treatment) for a 9 week recovery period. Transient clinical signs (lacrimation, blinking, decreased spontaneous motor activity) were reported on days 3-4 of treatment, and body weight was slightly decreased at week 13 in both sexes. There were no effects attributable to PDC in the functional observational battery, grip strength, or motor activity. Results from the gross and microscopic examination of the brain and nervous system revealed no treatment-related lesions. Overall, apart from a minor effect on body weight (NOAEL_{males} = 20 mg/kg bw/day; NOAEL_{females} 65 mg/kg bw/day), no adverse structural or functional neurological consequences were apparent in rats following 13 weeks gavage administration of PDC at doses up to 200 mg/kg bw/day. The effects of repeated (13 week) inhalation exposure to PDC were investigated in rats, mice, and rabbits (Nitschke *et al.*, 1988). This GLP compliant study evaluated macroscopic and microscopic effects following exposures to 15, 50, and 150 ppm for rats and mice and 150, 500, and 1000 ppm in rabbits. Nasal respiratory changes, considered site-of-contact effects, were identified in rats, and slight reductions in body weight were also reported (NOEL of 15 ppm for both). No effects whatsoever were identified in mice (NOEL of 150 ppm). Results from rabbits demonstrated slight changes in red blood cell parameters, which were

indicative of a macrocytic normochromic, regenerative anemia (LOEL of 150 ppm for males; NOEL of 150 ppm for females).

Overall, results from repeat dose studies indicate that the liver is a target organ in rodents with a chronic oral NOAEL of 62-125 mg/kg bw/d in rats and a chronic LOAEL of 125 mg/kg bw/d in mice (no NOAEL established). There were no adverse systemic effects in rats and mice following subchronic exposure to 150 ppm PDC (NOAEL), whereas red blood cell parameters (regenerative anemia) were altered in rabbits with a LOAEL of 150 ppm in males and a NOAEL of 150 ppm in females. Body weight was slightly but statistically significantly decreased in rats only (NOAEL 15 ppm) in these sub-chronic inhalation studies, with site-of-contact (irritative) changes present in stomach (mouse, NOAEL/LOAEL 125 mg/kg bw/d after oral gavage, dependent on sex) and nasal tissue (rat, NOAEL 15 ppm after inhalation). The toxicity profile has been well-studied and documented. **No additional testing required.**

Summary of repeat oral toxicity data for 1,2-dichloropropane in rats and mice (gavage administration)

Species	Treatment	NOAEL / LOAEL	Comments
		(mg/kg bw/day)	
Rat	0, 125, 250, 500, 1000 or 2000	NOAEL = 500	All high-dose rats died during the study, with 15% decrease in bw at 1000 mg/kg bw/day (both
	$mg/kg \ bw/d \ for \ 2 \ wk$ $(n = 5/sex/dose)$		sexes). Reddening of the renal medullae (1000 mg/kg bw/day) was the only other toxicologically- relevant effect.
	0, 60, 125, 250, 500 or 1000	NOAEL = 250	All high dose animals and 50% of males given 500 mg/kg bw/day died early. Body weight decreased
	$mg/kg \ bw/d \ for \ 13 \ wk$ (n = 10/sex/dose)		8-16% in 500 mg/kg bw/day groups. Centrilobular congestion, hepatic fatty change and centrilobular necrosis, affecting up to 50% of high dose animals, seen microscopically.
	Males: 0, 62 or 125 mg/kg bw/day for 103 wk	$NOAEL_{males} = 62$	Survival of high dose females was significantly decreased relative to low dose and control groups (males unaffected). Body weight decreased 14-24% in high dose animals (both sexes). An increased
	Females: 0, 125 or 250 mg/kg	$NOAEL_{females} = 125$	incidence of hepatic foci of clear change and liver necrosis (high dose females only) were the only
	bw/day for 103 wk $(n = 50/sex/dose)$		lesions of note.
Mouse	0, 125, 250, 500, 1000 or 2000	$NOAEL_{males} = 250$	All high-dose mice died during the study, high levels of mortality also noted at 1000 mg/kg (both
	mg/kg bw/d for 2 wk		sexes) and 500 mg/kg (males only). No impact on body weight of survivors. Reddening of the renal
	(n = 5/sex/dose)	$LOAEL_{females} = 125$	medullae common in higher dose groups (both sexes), high incidence in males given 500 mg/kg, single occurrence in all lower female dose groups.
	0, 30, 60, 125, 250 or 500 mg/kg	NOAEL = 500	Minor (3-5%, not clearly dose-related) reduction in body weight, no histopathological lesions
	bw/d for 13 wk		present.
	(n = 10/sex/dose)		
	0, 125 or 250 mg/kg bw/day for	LOAEL = 125	Survival of high dose females decreased relative to control (concurrent reproductive tract infection
	103 wk		considered cause by NTP), survival of males unremarkable. Hepatocytomegaly and hepatic focal
	(n = 50/sex/dose)		necrosis (low and high dose males), acanthosis of the stomach (high dose males, low and high dose
			females) and suppurative inflammation of the reproductive tract (all females, indicative of infection) were the only histopathological changes detected.
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2 Data from NTP (1986)

Genetic Toxicity: Gene Mutations and Chromosome Aberrations

IUCLID 5.5 and 5.6: The mutagenic potential of 1,2-dichloropropane has been evaluated in a large number of microbial tests in bacteria and fungi, both in the absence and in the presence of exogenous metabolic activation (summarized by IARC, 1999). Overall, results from these tests are mixed with both positive and negative studies and are represented in the following table.

Summary of mutagenicity findings for 1,2-dichloropropane in Salmonella typhimurium tester strains (from IARC, 1999).

strums (nom nate, 1999).					
SALMONELLA TESTER STRAIN	Result		Dose * μg/ml	Reference	
	Without S9	With S9			
TA100	+	+	5000	De Lorenzo <i>et al</i> . (1977)	
	-	-	565	Stolzenberg and Hine (1980)	
	+	+	2900	Principe et al. (1981) J Sci	
	(+)	-	5000	Haworth <i>et al.</i> (1983)	
TA1535	+	+	5000	De Lorenzo <i>et al</i> . (1977)	
	+	+	2900	Principe <i>et al.</i> (1981)	
	(+)	-	5000	Haworth <i>et al.</i> (1983)	
TA1537	-	-	5800	Principe <i>et al.</i> (1981)	
	-	-	1666	Haworth <i>et al.</i> (1983)	
TA1538	-	-	5800	Principe <i>et al.</i> (1981)	
TA98	-	-	5800	Principe <i>et al.</i> (1981)	
	-	-	5000	Haworth et al. (1983)	
TA1978	-	-	25000	De Lorenzo <i>et al</i> . (1977)	

^{+ =} positive result;

However, in a GLP-compliant study with liquid pre-incubation conducted by the US National Toxicology Program, no mutagenic activity or cytoxicity was detected when PDC (up to $2000 \,\mu\,g$ /plate) was incubated with four strains of *Salmonella typhimurium* (TA 98, TA 1537, TA 100, TA 1535) in the absence or presence of S9 fraction from Arochlor 1254-induced rats (NTP, 1986). A satisfactory response was obtained with the positive control substances, benzo(a)pyrene and MNNG. PDC was also not cytotoxic or mutagenic in these same tester strains when evaluated in the absence or presence of S9 using a plate incorporation methodology (up to 3150 $\mu\,g$ /plate, in the absence or presence of glutathione supplementation; Oesch, 1979). Exposure to PDC vapor (atmosphere generated by evaporation of 0.3 - 10 ml of test

^{(+) =} weakly positive (inconsistent response between independent repeats; <2-fold increase);

^{- =} negative

^{*} Either lowest effective dose (for positive study) or highest ineffective dose (for negative study)

substance in a 201 dessicator) also failed to produce a response in the organisms in the presence or absence of S9 and glutathione supplementation (Oesch, 1979), whereas dichloroethane (3 ml) was positive in TA100 and TA1535 under these same conditions.

Overall, PDC has returned consistently negative results in *Salmonella typhimurium* tester strains TA1537 and TA98 at up to $5800~\mu$ g/ml in the absence or presence of S9, whereas TA100 and TA1535 have returned inconsistent results under similar conditions.

When tested in mammalian cells *in vitro*, no mutation at the thymidine kinase locus was detected in L5178Y cells after incubation with up to 1000 nl/ml 1,2-dichloropropane in the absence of rat S9 (cytotoxic at >800 nl/ml), while assays in the presence of S9 provided evidence of mutagenicity at or around the threshold for cytotoxicity (80 nl/ml) (Myhr and Caspary, 1991). In an assessment of clastogenic potential, the number of chromosomal aberrations present in CHO cells exhibited a dose-related response (reported as a 5- or >16-fold increase) after incubation with 1370 or 1580 μ g/ml PDC in the absence of S9, and an approximate 4-fold increase in the number of aberrant cells exposed to 660 or 950 μ g/ml in the presence of S9 (NTP, 1986). In another series of *in vitro* experiments, CHO cells exhibited a dose-related increase in sister chromatid exchanges after exposure to PDC *in vitro*, with an approximate doubling in response after incubation with 376 or 1127 μ g/ml PDC, both in the presence and absence of Arochlor 1254-induced rat S9 (NTP, 1986).

Results from a recent GLP compliant OECD 474 guideline mouse micronucleus study demonstrated no evidence of cytogenetic damage in bone marrow from CD-1 mice given up to 600 mg/kg bw by gavage (com oil vehicle) on 2 consecutive days (Spencer *et al.*, 2003). Systemic toxicity (2° C drop in body temperature) was noted in high dose animals, while results from the range-finder investigation indicated that higher treatment levels (1000 mg/kg bw and above) were lethal. A satisfactory response was obtained with the positive control substance (cyclophosphamide). Based on toxicokinetic data demonstrating PDC is distributed evenly across all tissues, including bone, exposure of the bone marrow can be assumed for this study. The results demonstrate no potential for PDC to damage genetic material present in immature red blood cells.

Similarly, negative results were also reported from a modern, guideline rat dominant lethal assay (Hanley *et al.*, 1989) performed to GLP. Male SD rats (n = 30/group) received PDC in drinking water at doses equivalent to 0, 28, 91 or 162 mg/kg bw/day for at least 13 wk. The high dose was a saturated solution of PDC in water. They were then mated with untreated females for two successive one-week periods. A positive control group (cyclophosphamide, 100 mg/kg bw, 48 hr prior to mating) was included in the study. Mating and fertility indices were comparable between the control and PDC-treated groups (96-100%), but decreased significantly in the positive controls. Slight variations in number of corpora lutea, number of implantations, pre-implantation losses and resorptions rates were noted in the first or second week of mating in the low and high dose groups (mid-dose group not different from control), but the magnitude of the change was within the normal control ranges. In contrast, the positive control group showed a 2-fold increase in pre-implantation loss and a 10-fold increase in resorption rate. Overall it was concluded that PDC had no capacity to induce heritable mutations in male SD rats following at least 13-week oral treatment with up to 162 mg/kg bw/day.

Overall while findings from *in vitro* genotoxicity tests are inconsistent, including both positive and negative findings in bacterial and mammalian systems, results from recent GLP compliant guideline investigations demonstrate that PDC is not a somatic or germ cell genotoxicant *in vivo*, despite widespread distribution throughout the body. In addition, results from adequate carcinogenicity assays in rats and mice provide supplementary information on the mutagenic potential of 1,2-dichloropropane *in vivo*. The findings (limited to liver tumours in mice and no convincing evidence of carcinogenicity in the rat) indicate that the compound is not a genotoxic carcinogen. **No additional testing is required.**

Carcinogenicity

IUCLID 5.7: The carcinogenic potential of PDC has been investigated in two long term oral gavage studies using F344 rats and B6C3F1 mice (NTP, 1986). Due to poor survival, statistical analysis of tumor incidence was adjusted for survival in both species.

No significant or treatment-related increase in tumor incidence was observed in male rats given 0, 62 or 125 mg/kg bw/day for 103 wk. Female rats given 125 or 250 mg/kg bw/day showed a positive trend for mammary adenocarcinoma incidence (adjusted rates: 3%, 5%, 27%), which was increased significantly in the high dose group. These were neither metastatic, anaplastic, nor highly invasive and were diagnosed by some NTP pathologists as highly cellular fibroadenomas (NTP, 1986). Affected high dose females showed a marked decrease in survival (32% alive at study end versus 74%-86% in the control and low dose groups) and a significant reduction (>20%) in body weight, suggesting that 250 mg/kg bw/day was in excess of the Maximum Tolerated Dose for PDC; compromised metabolic, immune, or hormonal status was possible under such conditions (NTP, 1986). It is pertinent that there was no increase in liver tumors despite the occurrence of chronic histopathological changes, including foci of clear change and necrosis. Based on these findings, NTP concluded that there was no evidence for the carcinogenicity of PDC in male rats, while in females given 250 mg/kg bw for 103 wk, there was equivocal evidence of an increased incidence of mammary adenocarcinoma; these were considered borderline malignant lesions by NTP, which occurred concurrently with decreased survival and reduced body weight gain. In mice, there was a positive trend for liver adenoma (adjusted for survival) in both sexes given 0, 125, or 250 mg/kg bw/day for 103 weeks. Tumor incidences in high dose males (45%) and both groups of treated females (17-19%) were increased significantly relative to the controls (20% in males, 3% in females). The findings in male mice occurred in the presence of hepatocytomegaly and hepatic focal necrosis in both treatment groups. The incidence of liver tumors in female mice was essentially identical in the two treated groups, despite a 2-fold difference in dose. High dose females also showed an increased incidence of thyroid tumors but this was not clearly dose-related (combined follicular cell carcinomas and adenomas, adjusted rates 3%, 0%, or 21% in control, low, and high dose groups), and occurred in the presence of liver changes (hepatocytomegaly, focal necrosis, tumors), which may have affected the metabolic and/or hormonal status of the animals. Body weights (both sexes) were unaffected by treatment, while survival at week 103 was reduced in treated females due to reproductive tract infection (70%, 58% and 52% for control, low and high dose animals; males unremarkable). NTP concluded that there was some evidence of carcinogenicity for PDC in male and female mice, based upon an increased

incidence of hepatocellular neoplasms, primarily adenomas (thyroid tumors disregarded). While the mechanism underlying these changes is unknown, the occurrence of histopathological liver lesions in male mice (LOAEL 125 mg/kg bw/day) suggests that chronic target organ toxicity may have played a contributing role in the expression of these benign tumors.

Hepatocellular adenoma is a common finding in control B6C3F1 mice. Historical control data for this lesion from contemporaneous NTP studies conducted to 1995 (corn oil, gavage, 16 studies) returned an incidence of 267/813 (33%) in males (range 14-58%) and 111/809 (14%) in females (range 2-28%) (Analytical Services Inc, 1995). Comparison of this historical control information with findings from the NTP study shows that the control incidence for males and females from this study (20%, 3%, respectively) was lower than the mean historical control data, while the incidence for high dose males (45%) and both treated females groups (17%, 19%) was below the upper bound of the historic control data. Spontaneous biological variation in the control data may therefore have influenced the results of this study. When reviewing the rat and mouse tumor findings reported by NTP, IARC (1999) concluded that 1,2-dichloropropane is not classifiable as to its carcinogenicity to humans (Group 3). Overall, these considerations indicate that PDC is not a directacting carcinogen, that there is equivocal evidence of an increase in mammary tumors in female rats, and that other factors (such as spontaneous biological variation) may have contributed to the increased incidence of mouse liver tumors.

No additional testing is required.

Reproductive Toxicity

IUCLID 5.8: The effect of PDC on the reproductive performance of male and female S-D rats was investigated in a GLP-compliant, guideline, 2-generation study by Kirk *et al.* (1990). PDC was administered in drinking water at levels of 0%, 0.024%, 0.1% or 0.24% (w/v), equivalent to received doses of 20-30, 70-130 or 130-250 mg/kg bw/day, respectively, for the parental generations; females received higher doses during lactation, equivalent to approx. 60, 200 and 450-500 mg/kg bw/day. Water consumption was decreased 20-50% in the mid- and high dose groups, possibly reflecting poor palatability linked to the presence of PDC. Gestational body weight gain was reduced by approximately 20% in high dose dams and 7-13% in mid dose females. Treatment-related hepatocellular granularity,

considered an adaptive change by the study pathologist, was present in males and females of both generations at all dose levels (incidence in high dose animals: ≤17% in females; <13% for males). All other tissues, including reproductive organs from both sexes, were unremarkable. Despite the observed effects, reproductive function was unaffected in males and females of both generations. Although neonatal body weight was decreased, and neonatal mortality greater, in litters from high-dose dams consuming up to 250 mg/kg bw/d during pregnancy or up to 500 mg/kg bw/d during lactation, this appears secondary to maternal dehydration and a 20% reduction in gestational body weight gain, rather than a direct effect on reproduction. Live births, litter sizes and other pup parameters were unremarkable. Based on these findings, the study demonstrated a parental NOAEL of 20-30 mg/kg bw/day (0.024%; based upon body weight effects), a NOAEL in the offspring of 70-130 mg/kg bw/day (0.1%), and a reproductive NOAEL of 130-250 mg/kg bw/day (0.24%). Overall this study provides no evidence that PDC selectively targets the male or female reproductive system. No additional testing is re quired

Developmental Toxicity

IUCLID 5.9: The potential effects of PDC on embryonal/fetal development were investigated in two species by Kirk *et al.* (1995) in two GLP-compliant guideline studies. Pregnant S-D rats were treated with 0, 10, 30 or 125 mg/kg bw/day PDC in corn oil (gavage) on gestation days 6·15 inclusive and fetuses examined on GD 20, while pregnant New Zealand White rabbits received 0 (corn oil vehicle), 15, 50 or 150 mg/kg bw/day on GD 7-19, inclusive, followed by a fetal examination on GD 28.

Clear signs of maternal toxicity were present in high dose animals of both species. Rats given 125 mg/kg bw/day exhibited clinical signs (decreased movement and muscle tone, lacrimation, salivation) on GD 6 and 7, with an approx. 25% reduction in food and water consumption and a 30% reduction in body weight gain over the entire treatment period. Rabbits given 150 mg/kg bw/day showed a statistically significant net reduction in mean body weight gain on GD 7-20 (decreased 165 g) while controls showed a net gain (49 g) during the same period. Haematological changes were also noted in high dose rabbits (not evaluated in rats), with an approx. 20% reduction in red cell counts, haemoglobin concentration and haematocrit, while platelet and white cell counts were increased by 20-25%. Fetal examination revealed

a similarly low incidence of variations in control and treated groups of both species; the only treatment-related finding was a significant increase in delayed ossification of the bones of the skull in high dose rats and rabbits, indicative of a developmental delay. There was no evidence of any teratogenic effect. The NOAELs from this study are summarised in the following table.

Maternal and fetal NOAELs

	NOAEL (mg/kg bw/day)		
	Rat	Rabbit	
Maternal toxicity	30	50	
Fetal toxicity	30	50	
Teratogenicity	125	150	

Overall, results from these well-conducted developmental toxicity studies demonstrated the occurrence of mild fetotoxicity (delayed ossification) coincident with maternal toxicity. PDC was not teratogenic under the conditions of these investigations. **No additional testing is required**

V CONCLUSIONS

Evaluation of the existing data leads to the conclusions that a substantial quantity of data currently exist to adequately represent the toxicological and ecological screening profile of CAS 63890-96-5 C3 Chlorinated Hydrocarbon Stream, and these data support the conclusion that **no further testing is needed to satisfy endpoints for HPV/SIDS.**

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Summary of Endpoints and Data Quality

	PDC (78-87-5)	Adequacy	GLP?	Required Testing?
PHYSICAL CHEMISTRY				
Melting point, °C	-70°C	A_{calc}	No data	No
Boiling point, °C	95-96°C @ 1013hPa	A_{calc}	No data	No
Vapor Pressure @ 20°C	66.2 hPa	A_{calc}	No data	No
Water Solubility @ 25°C	2800 mg/m ³	A_{exp}	No data	No
Log K _{ow}	2.0	A_{calc}	No data	No
Density	1.155 g/cm ³ @ 20°C	A_{exp}	No data	No
ENVIRONMENTAL FATE				
Biodegradation	Not readily biodegradable	A_{exp}	Yes	No
Hydrolysis	½ Life at pH 7 ~ 15.8 years	A_{calc}	No data	No
Photodegradation	Does not absorb light at 290nm	A_{calc}	No data	No
Transport between Environmental Compartments: (Fugacity Level III Mode) Default assumption: 1000 kg/hr released simultaneously into air, water, and soil.	98.85% to air 0.93% to water 0.21% to soil <0.01% to sediment	A_{calc}	No data	No
ECOTOXICITY				
Acute Toxicity to Fish (LC ₅₀)	LC ₅₀ (96h)=140 mg/L in Pimephales promelas	A_{exp}	No Data	No
Acute Toxicity to Aquatic Invertebrates (48hr EC ₅₀)	$EC_{50} = 55.9 mg/L for$ immobilization of Daphnia magna	A_{exp}	Yes	No
	28-day NOEC = 4.1 mg/L in Mysidopsis bahia	A_{exp}	Yes	
Toxicity to Aquatic Plants	In Skeletonema costatum: 72-hour $EC_{50} = 14.7 - 15.8$ mg/L	A_{exp}	Yes	No
	$NOEC_{120hour} = 7.4 - 8.9$ mg/L			
TOXICOLOGICAL DATA				
Acute Toxicity (oral)	$LD_{50} = 2200 \text{ mg/kg in}$ Wistar rats	A_{exp}	No	No
Acute Toxicity (dermal)	LD ₅₀ > 10,100 mg/kg in rabbits	A_{exp}	No	No
Acute Toxicity (inhalation)	4 -hour $LC_{50} = 2000ppm$	A_{exp}	No	No

	(9.4mg/L) in rats			
	7-hour LC ₅₀ > 2200ppm (10.3 mg/L) in rats	A_{exp}	No	
	7-hour LC ₅₀ > 2200ppm (10.3 mg/L) in Guinea pigs	A_{exp}	No	
Acute Skin Irritation	In rabbits, a slight irritant	A_{exp}	Yes	No
Acute Eye Irritation	Redness, oedema, and slight opacity in rabbits, resolved at day 8.	A_{exp}	No	No
Sensitization	Negative in the LLNA / Positive in questionable human patch tests	A_{exp}	Yes / No	No
Repeated Dose Toxicity	Subchronic NOAEL = 250 mg/kg/day in rats	A_{exp}	Yes	No
	Chronic NOAEL = 62-125 mg/kg/day in rats	A_{exp}	Yes	
	Subchronic NOAEL = 250 mg/kg/day male mice, LOAEL = 125 mg/kg/day female mice	A_{exp}	Yes	
	Chronic LOAEL = 125 mg/kg/day in mice	A_{exp}	Yes	
Genetic Toxicity-Mutation	Results of tests are mixed. See text table.	A_{exp}	Yes / No	No
Genetic Toxicity- Chromosomal Aberrations	Results of tests are mixed. See text table.	A_{exp}	Yes / No	No
Toxicity to Reproduction	Reproductive function was unaffected in males and females of 2 generations; Parental NOAEL = 20-30 mg/kg/day; offspring NOAEL = 70-130 mg/kg/day; reproductive NOAEL = 130-250 mg/kg/day	A_{exp}	Yes	No
Developmental Toxicity	Mild fetotoxicity (delayed ossification) coincident with maternal toxicity in rats & rabbits. See text table for NOAEL's	A_{exp}	Yes	No

TEST =Testing required to fill data gap

NA = Not applicable due to physical / chemical properties

calc = Value determined by calculation or estimation

 $_{\text{Exp}} = \text{Data derived via experimentation}$

IUCLID

Data Set

Existing Chemical : ID: 78-87-5 CAS No. : 78-87-5

EINECS Name : 1,2-dichloropropane

EC No. : 201-152-2

TSCA Name : Propane, 1,2-dichloro-

: C3H6Cl2 Molecular Formula

Producer related part

Company : Dow Chemical, TERC

Creation date : 05.10.2004

Substance related part

: Dow Chemical, TERC Company

05.10.2004 **Creation date**

Status

Memo PDC File originally from AK Mallett

Printing date 14.12.2004 Revision date

Date of last update 14.12.2004

Number of pages : 202

Chapter (profile) : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10 Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4

Flags (profile) : Flags: without flag, confidential, non confidential, WGK (DE), TALuft (DE),

Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

ld 78-87-5 **Date** 14.12.2004

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : lead organisation

Name : Dow Chemical Company

Contact person : Dr. W.T. Stott, Dr. L.H. Pottenger

Town : MI 48674 Midland, Michigan

Country : United States
Phone : +1-989-636-1000

Telefax :
Telex :
Cedex :
Email :
Homepage :

Remark : Please, send all comments and questions to Dr. W.T. Stott or Dr. L.H.

Pottenger, Dow Chemical Company, 1803 Bldg., Midland-USA

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

14.12.2004

Type : cooperating company
Name : EC Erdoelchemie
Contact person : Dr. C. Gabel
Date : 11.05.1994

Street: Produktionsabteilung VII SUU / Postfach 75 20 02

Town : D-50754 Koeln Country : Germany

Phone

Telefax

Telex Cedex

Email

Homepage :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

26.10.2004

Type : cooperating company

Name : Enichem S.p.A, Polyurethane Division

Contact person : Dr. M. Vasta Date : 11.05.1994

Street : Via Delle Roccette 36
Town : I-21010 Cardano Al Campo

Country : Italy

Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

26.10.2004

Type : cooperating company
Name : Solvay & Cie
Contact person : Mr. A. Berends

Date : 11.05.1994

ld 78-87-5 **Date** 14.12.2004

Street : Rue du Prince Albert, 33
Town : B-1060 Bruxelles

Country : Belgium

Phone :

Telefax :
Telex :
Cedex :
Email :
Homepage :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

26.10.2004

Type : cooperating company
Name : Asahi Glass Company, Ltd.

:

:

Contact person : Dr. Katsuji-Itoh

Date

Street Town

Country Phone

Telefax : Telex : Cedex :

Email : katsuji-itoh@om.agc.co.jp

Homepage

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

26.10.2004

Type : manufacturer

Name : Contact person :

 Date
 :

 Street
 :

 Town
 :

 Country
 :

 Phone
 :

 Telefax
 :

 Telex
 :

 Cedex
 :

 Email
 :

 Homepage
 :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

26.10.2004

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

ld 78-87-5 **Date** 14.12.2004

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type

Substance type: organicPhysical status: liquidPurity: > 99 % w/w

Colour

Odour : sweet, chloroform-like

Remark : stable; colorless

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,2-Dichlorpropan

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

06.01.1994

alpha, beta-Dichloropropane

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

alpha, beta-Propylene dichloride

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Dichloro-1,2-propane

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Dichloropropane

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Propane, 1,2-dichloro

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Propylenchlorid

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Propylendichlorid

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

ld 78-87-5 **Date** 14.12.2004

Propylendichlorid-1,2

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Propylene chloride

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

13.12.1993

Propylene dichloride

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

1.3 IMPURITIES

Purity : CAS-No : EC-No :

EINECS-Name : oxygenated organic substances

Molecular formula

Value : < .4 % w/w

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

Purity :

 CAS-No
 : 67-64-1

 EC-No
 : 200-662-2

 EINECS-Name
 : acetone

Molecular formula

Value : < .1 % w/w

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

Purity

CAS-No : 123-38-6 EC-No : 204-623-0 EINECS-Name : propionaldehyde

Molecular formula

Value : < .1 % w/w

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

Purity

CAS-No : 7732-18-5 **EC-No** : 231-791-2 **EINECS-Name** : water

Molecular formula

Value : <= .02 % w/w

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

ld 78-87-5 **Date** 14.12.2004

1.4 ADDITIVES

Remark : no additives

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

1.5 TOTAL QUANTITY

Quantity : 480000 - 530000 tonnes produced in 2001

Remark: Volume refers to production globally

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (1) (2) (3) (4)

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC

Nota :

R-Phrases : (11) Highly flammable

(20/22) Harmful by inhalation and if swallowed

S-Phrases : (16) Keep away from sources of ignition - No smoking

(24) Avoid contact with skin

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (5)

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC

Class of danger : harmful

R-Phrases : (20/22) Harmful by inhalation and if swallowed

Specific limits :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004

Classified : as in Directive 67/548/EEC

Class of danger : highly flammable R-Phrases : (11) Highly flammable

Specific limits :

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

20.06.2000 (5)

1.6.3 PACKAGING

ld 78-87-5 **Date** 14.12.2004

1.7 USE PATTERN

Type of use : use

Category : Intermediates

Remark: Used as an intermediate in the production of chlorinated

solvents (perchloroethylene/tetrachloroethylene).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (6)

Type of use : industrial

Category : Basic industry: basic chemicals

Remark : 1,2-dichloropropane was used as a solvent for oil, fats,

caoutchouc, gum, wax and resins and also as a textile spot remover, paraffin remover, scrubbing agent ingredient, cleanser and a galvanizer. As bitumen, asphalt and tar dissolves easily in 1,2-dichloropropane it was used to

manufacture construction aides and roofing.

1,2-dichlorpropane is no longer used in Western Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (7) (8) (9)

Type of use : type

Category : Non dispersive use

Remark: 1,2-dichloropropane is and was used as a nematicide,

insecticide and pesticide. Formulations of

1,2-dichloropropane and 1,3-dichloropropene are used.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (10) (11) (12) (8) (13) (14) (9)

Type of use : industrial

Category : Agricultural industry

Remark: 1,2-dichloropropane was used as a nematicide,insecticide and

pesticide. Commercial products such as Telone II or D-D

contains 94 % 3-dichloropropene and 0,2 %

1,2-dichloropropane or 52 % 1,3-dichloropropene and 29 % 1,2-dichloropropane. At this time in the German Republic (BRD) 1,2-dichloropropane in pesticides is not allowed and

is not on the market.

This use type is discontinued in the U.S. and the EU. Status

in other OECD countries is unclear.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (7) (15) (16) (17)

Type of use : industrial

Category : other: flame retardants and fire preventing agents

Remark : 1,2-dichloropropane is used as a flame retardant during the

manufacture of flame retardant rubber mixtures. It is

also applied as an impregnation agent.

This cited application needs further investigation as PDC is

highly flammable!

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (8) (18)

Type of use : use

ld 78-87-5 **Date** 14.12.2004

Category : Fuel additives

Remark: 1,2-dichloropropane is used as a lead additive in fuel

additives. Given the reduction in use of leaded fuels, this

use is minor.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (19)

Type of use : use Category : Pesticides

Remark: 1,2 dichloropropane has been used as a nematicide,

insecticide and pesticide. Formulations of

1,2-dichloropropane and 1,3-dichloropropene are applied to

the above.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (10) (11) (12) (8) (13) (14) (20)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAC (NL) Limit value : 350 mg/m3

Country : Netherlands

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (21)

Type of limit : MAK (DE) Limit value : mg/m3

Country : Germany

Remark: No MAK-value is given. Dichloropropane is in the

carcinogenic group IIIB, i.e. the compound is possibly

expected to have carcinogenic potential.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (22)

Type of limit : other: ACGIH TLV (US)

Limit value : 347 mg/m3

Short term exposure limit value

Limit value: 508 mg/m3Time schedule: 15 minute(s)Frequency: 4 times

Country : USA

Remark : Dichloropropane is identified by other sources as a possible

human carcinogen.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (23)

ld 78-87-5 **Date** 14.12.2004

Type of limit : other: Odor Threshold limit in air

Limit value : 420 mg/m3

Country : USA

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (24)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : Production process:

Propylenedichloride is a co-product of the chlorohydrin process during the production of propylene oxide and of

alkylchloride.

Emission:

The existing exposure guidelines are strictly followed

during production.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (6)

1.11 ADDITIONAL REMARKS

Remark : Water Pollution

.....

Classified by : KBwS (DE) Labelled by : KBwS (DE)

Class of danger: 3 (strongly water polluting)

Country: Germany

Classified by : EU Commission

Id 78-87-5 Date 14.12.2004

Labelled by : EU Commission

Class of danger: -Country : EU

Remark : The European Union added 1,2-dichloro-

propane to the "black list", which

contains

129 substances of high priority chemicals. 1,2-dichloropropane is one of the 83 substances of this list with special significance for the Rhine River tributaries. At the same time these 83 substances also entered the research program of the International Rhine

Commission.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (25)(26)

Remark Major Accident Hazards

Legislation : Stoerfallverordnung (DE)

Substance listed: yes Country : Germany

Remark : appendix II, Number 114

Legislation : Gefahrgutverordnung Binnenschiffahrt

(GGVBinSch)

Substance listed: yes Country : Germany

Remark : class 3, Number 1a

Legislation : Gefahrgutverordnung Eisenbahn (Reglement

international concernant le transport des

marchandises dangereuses par chemins de

fer/Accord europeen relatif au

transport international des marchandises dangereuses par route, RID (GGVE)

Substance listed: yes

Remark : class 3, Number 3b

Legislation : Gefahrgutverordnung See (GGVSee)

Substance listed: yes Remark : class 3.2

Legislation : Gefahrgutverordnung Strasse (GGVS)

Substance listed: yes Country : Germany

Source

10.07.2000

Remark : class 3, Number 3b

: The 1,2-Dichloropropane ICCA/HPV Consortium

(27) (28) (29) (30) (31)

ld 78-87-5 **Date** 14.12.2004

Remark : Air Pollution

Classified by : TA-Luft (DE) Labelled by : TA-Luft (DE)

Class of danger: 1 Number: 3.1.7 (organic substances)

Country : Germany

Remark : 1,2-dichloropropane is not listed in

Appendix E of the "TA-Luft".

Corresponding to Nr. 3.1.7, paragraph 3 of the "TA-Luft" 1,2-dichloropropane was

added to class I. The emission

concentration of class I substances can not exceed 20 mg/m3 by a mass stream of

0.1 kg/h.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

08.08.2000 (32)

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

ld 78-87-5 **Date** 14.12.2004

2.1 MELTING POINT

Value : = -100.4 °C

Sublimation : Method : Year : GLP :

Test substance: as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (33)

Value : = -100.4 °C

Sublimation : Method : Year : GLP : :

Test substance: as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (34)

Value : =-100.4 °C

Sublimation

Method : other

Year :

GLP : no data

Test substance :

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

29.02.2004 (35)

Value : =-100 °C

Sublimation

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (36)

Value : =-100 °C

Sublimation :

ld 78-87-5 **Date** 14.12.2004

Method : other: not specified

Year

GLP : no data

Test substance

Remark: Freezing point;

Hazardous decomposition products: hydrogen chloride,

chlorine, phosgene

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (37)

2.2 BOILING POINT

Value : = 96.4 °C at

Decomposition : Method :

Year : 2001 GLP : no data

Test substance: as prescribed by 1.1 - 1.4

Remark : Experimental data judged acceptable by the AIChE (American Institute of

Chemical Engineers) DIPPR ENVIRON 2001 database.

Reliability : (2) valid with restrictions

2g-data from a handbook or collection of data.

20.10.2004 (38)

Value : $= 94 - 96.8 \, ^{\circ}\text{C}$ at

Decomposition

Method Year

GLP

Test substance : as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

(C) --- i'-l --- itl- --- -- t--i --ti

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

20.10.2004 (33)

Value : = 96.4 °C at

Decomposition : Method :

Year

GLP

Test substance : as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

20.10.2004 (34)

Value : = 96.4 °C at

Decomposition :

ld 78-87-5 **Date** 14.12.2004

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

20.10.2004 (35)

Value : = 96.8 °C at

Decomposition

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

20.10.2004 (39)

Value : $= 95 - 100 \, ^{\circ}\text{C}$ at

Decomposition

Method : other: DIN 53 171

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

20.10.2004 (37)

Value : = 96 °C at

Decomposition

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

20.10.2004 (36)

Value : = 96.5 °C at

Decomposition

Method : other: not specified

Year :

GLP : no data

Test substance :

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

20.10.2004 (20)

ld 78-87-5 **Date** 14.12.2004

Value : = 96.6 °C at

Decomposition

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

20.10.2004 (40)

2.3 DENSITY

Type : density

Value : = 1.155 g/cm³ at 20 °C

Method : Year :

GLP

Test substance : as prescribed by 1.1 - 1.4

Remark: Mean calculated value at 20 degrees C based on data from

MacKay et al. (1993).

Source : Dow Europe

DOW Europe Horgen
A.K. Mallett Surrey
(2) valid with restriction

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

01.03.2004 (33)

Type : density

Value : = 1.1494 - 1.16 at 20 °C

Method : Year :

GLP

Test substance: as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

01.03.2004 (33)

Туре

Value : = 1.156 g/cm³ at 20 °C

Method : other: not specified

Year

GLP : no data

Test substance :

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (35)

ld 78-87-5 **Date** 14.12.2004

Type

Value : = 1.159 g/cm³ at 25 °C

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (41)

Туре

Value : = 1.182 g/cm³ at 0 °C

Method : other: not specified

Year

GLP : no data

Test substance

Remark : ------

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

08.08.2000 (20)

Type : relative density

Value : = 1.16 g/cm³ at 20 °C

Method : other: not specified

Year

GLP : no data

Test substance

Remark: Density was measured in relation to water (water=1).

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (40)

Type : relative density

Value : = 1.16 g/cm³ at 20 °C

Method : other: not specified

Year :

GLP : no data

Test substance :

Remark : Density was measured in relation to air (air=1).

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

29.02.2004 (40)

Type :

ld 78-87-5 **Date** 14.12.2004

(33)

Value : = 1.166 g/cm³ at 20 °C

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (37)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 66.2 hPa at 25 °C

Decomposition : Method : Year : GLP :

Test substance: as prescribed by 1.1 - 1.4

Remark : Selected value (Mackay et al. 1993) = 66.2 hPa (25 degrees

C)

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

01.03.2004

Value : = 66.17 - 71.98 hPa at 25 °C

Decomposition : Method : Year : GLP :

Test substance: as prescribed by 1.1 - 1.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey (2) valid with restrictions

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (33)

Decomposition : Method : Year : GLP :

Test substance : as prescribed by 1.1 - 1.4

Remark: Vapour Pressure = 49.67 mm Hg at 25 degrees C

Source : Dow Europe

DOW Europe Horgen
A.K. Mallett Surrey

Reliability : (2) valid with restrictions

ld 78-87-5 **Date** 14.12.2004

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

29.02.2004 (34)

Value : = 13.3 hPa at -6.1 °C

Decomposition

Method : other (calculated): not specified

Year

GLP : no data

Test substance

Remark : ------

Temperature Vapour Pressure

19.4 53.3 hPa
25 66.7 hPa
39.4 133.3 hPa
76 533.2 hPa

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

28.04.1994 (42)

Value : = 18 hPa at $0 \, ^{\circ}$ C

Decomposition

Method : other (calculated): not specified

Year

GLP : no data

Test substance

Remark : ------

Temperature Vapour Pressure

20 51 - 56 hPa
50 198 hPa
80 599 hPa

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

08.08.2000 (43)

Value : 51 - 56 hPa at 20 °C

Decomposition

Method : other (calculated): not specified

Year

GLP : no data

Test substance

Remark : Ref. 1:

Temperature Vapour Pressure

20 51 - 56 hPa 25 66.7 hPa 30 88.0 hPa

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

ld 78-87-5 **Date** 14.12.2004

08.08.2000 (44) (45) (39)

Value : = 52.3 hPa at 20 °C

Decomposition

Method : other (calculated): not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (40)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water Log pow : = 2 at °C

pH value :
Method :
Year :
GLP :

Test substance: as prescribed by 1.1 - 1.4

Remark : Selected value (Mackay et al. 1993) Log Kow = 2.00

(temperature not stated)

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

11.10.2004 (33)

Partition coefficient : octanol-water Log pow : = 1.99 - 2.28 at °C

pH value :
Method :
Year :
GLP :

Test substance: as prescribed by 1.1 - 1.4

Remark : Temperature of determination not available.

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

01.03.2004 (33)

Partition coefficient : octanol-water Log pow : = 1.99 at °C

pH value :
Method :
Year :
GLP :

Test substance : as prescribed by 1.1 - 1.4

Source : Dow Europe

ld 78-87-5 **Date** 14.12.2004

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

01.03.2004 (34)

Partition coefficient

Log pow : = 1.99 at °C

pH value

Method : other (calculated): according to Pomona-MedChem-Strukturfragment

Method

Year :

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.06.2000 (40)

Partition coefficient :

Log pow : = 2 at °C

pH value

Method : other (calculated): according to Hansch & Leo (1979)

Year : GLP :

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

23.06.2000 (8)

Partition coefficient

Log pow : = 2.02 at °C

pH value

Method : other (calculated): according to Hansch & Leo (1979)

Year :

GLP :

Test substance :

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

23.06.2000 (46)

Partition coefficient

Log pow : = 2.02 at °C

pH value

Method : other (calculated): Computer calculation according to fragment method

Year :

GLP :

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.06.2000 (47)

Partition coefficient

Log pow : = 2.16 at °C

Id 78-87-5 Date 14.12.2004

pH value

Method other (calculated): according to Rekker (1977)

Year **GLP**

Test substance

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

23.06.2000 (48)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water

Value : = 2800 other:mg/m3 at 25 °C

pH value

concentration at °C

Temperature effects

Examine different pol.

: at 25 °C

Description Stable

Source : Dow Europe

> DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

: Critical study for SIDS endpoint Flag

11.10.2004 (33)

Solubility in Water

Value = 2.8 g/l at 20 °C

pH value

concentration at °C

Temperature effects

Examine different pol. :

pKa : at 25 °C

Description

Stable

: Dow Europe Source

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

:

Data from handbook or collection of data.

11.10.2004 (45)

Solubility in

Value = 2.7 g/l at 20 °C

рΗ value

concentration at °C

Temperature effects

Examine different pol.

pKa at 25 °C

Description

Stable

Deg. product

Method : other: not specified

Year

ld 78-87-5 **Date** 14.12.2004

GLP : no data

Test substance :

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

11.10.2004 (40) (39)

Solubility in : Water

Value : = 2740 mg/l at 25 °C

pH value

concentration : at °C

Temperature effects

Examine different pol. :

pKa : at 25 °C

Description

Stable

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

11.10.2004 (34)

Solubility in

Value : = 3 g/l at 20 °C

pH value

concentration : at °C

Temperature effects

Examine different pol. :

pKa : at 25 °C

Description Stable

Deg. product

Method : other: not specified

Year

GLP : no data

Test substance :

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

11.10.2004 (37)

2.6.2 SURFACE TENSION

Source : DOW Europe Horgen

A.K. Mallett Surrey

09.05.2003

2.7 FLASH POINT

Value : =21 °C

ld 78-87-5 **Date** 14.12.2004

Type : open cup Method : other: DIN 51758

Year :

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

29.02.2004 (41)

 Value
 : = 13 °C

 Type
 : closed cup

 Method
 : other: DIN 51755

Year GLP

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

06.01.1994 (49)

 Value
 : = 15 °C

 Type
 : closed cup

 Method
 : other: DIN 51755

Year : GLP : Test substance :

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

08.08.2000 (20)

Value : = 16 °C

Type : closed cup

Method : other: not specified

Year :

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (40)

2.8 AUTO FLAMMABILITY

Value : = 555 °C at

Method : other: not specified

Year

GLP : no data

Test substance

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

a maneta came,

Id 78-87-5 Date 14.12.2004

Reliability (2) valid with restrictions

11.10.2004 (50)

Value $= 557 \, ^{\circ}\text{C}$ at

Source : Dow Europe

> DOW Europe Horgen A.K. Mallett Surrey

: (2) valid with restrictions Reliability

Data from a handbook

11.10.2004 (19)

=600 °C at Value

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

Reliability (2) valid with restrictions

Data from a handbook

11.10.2004 (51)

Value = °C at Method

other: DIN 51 794

Year

GLP no data

Test substance

Remark Auto-ignition temperature > 200 degrees C

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

24.07.2000 (37)

2.9 **FLAMMABILITY**

Result flammable

Method other: not specified

Year

GLP no data

Test substance

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

28.04.1994 (50)

Result other: flammability limits Method other: not specified

Year

GLP no data

Test substance

Remark Upper and lower flammability limits are 12.2 (at 50 degrees

C) and 3.2 %vol/vol, respectively.

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

24.07.2000 (40)

ld 78-87-5 **Date** 14.12.2004

2.10 EXPLOSIVE PROPERTIES

Result : other: explosive

Remark: Highly flammable vapors of 1,2-dichloropropane together with

air are explosive. This mixture is heavier than air.

Explosion limit (Vol.-%) at 20 degrees C:

upper limit: 14.5 lower limit: 3.4

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

08.08.2000 (44) (50) (51)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Remark: Vapor density: 3.9 kg/m3

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

A.K. Maliett Surre

08.08.2000 (39)

Remark: relative vapor density: 3.89 (air = 1)

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

29.06.2000 (40)

Remark : Thermal energy at 304 degrees C, 44300 hPa: 308.0 kJ/kg

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

08.08.2000 (20)

Remark: Thermal energy: 312.1 kJ/kg

Source : Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

24.07.2000 (35)

Remark : Specific temperature at 30 degrees C: 1.38 kJ/kg x K

Source : Dow Europe

DOW Europe Horgen

Id 78-87-5 Date 14.12.2004

A.K. Mallett Surrey

08.08.2000 (20)

Remark Solubility of water in 1,2-dichloropropane at 20 degrees C:

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

08.08.2000 (20)

Remark : 1,2-dichloropropane is soluble in ethanol, diethylether,

benzol and chloroform.

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

29.06.2000 (35)

Azeotropic mixtures (at 1013 hPa): Remark

> 1,2-dichloropropane boiling point weight-%

> with (degrees C) 1,2-dichloropropane

in the azeotrope

78.0 90 water

methanol 62.9 47

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

08.08.2000 (20)

Remark Azeotropic mixtures (at 1013 hPa):

1,2-dichloropropane boiling point weight-% with (degrees C) 1,2-dichloropropane

in the azeotrope 42.3

ethanol 74.7 80.4 16 cyclohexane 76.6 16 tetrachloromethane

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

24.07.2000 (49)

Remark Surface tension at 20 degrees C: 0.03 N/m

Source Dow Europe

> DOW Europe Horgen A.K. Mallett Surrey

08.08.2000 (20)(52)

Remark : viscosity (mPa x s):

at 0 degree C 1.2 at 20 degrees C 0.85 at 50 degrees C 0.58

at 80 degrees C 0.44

Source Dow Europe

DOW Europe Horgen

A.K. Mallett Surrey

08.08.2000 (20)

ld 78-87-5 **Date** 14.12.2004

3.1.1 PHOTODEGRADATION

Type : air Light source :

Light spectrum : nn

Relative intensity: based on intensity of sunlight

Deg. product : Method : Year : GLP :

Test substance: as prescribed by 1.1 - 1.4

Remark: Photo-oxidation half-life in air. based on estimated rate

constant for the vaour phase reaction with hydroxyl radicals

in air, in the range 65 - 646 hr.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

25.10.2004 (33)

Type : air Light source :

Light spectrum : nm

Relative intensity: based on intensity of sunlight

Deg. product

Method Year GLP

Test substance : as prescribed by 1.1 - 1.4

Remark : 1,2-Dichloropropane does not have any chromophores that

absorb wavelengths >290 nm, so direct photolysis will not be

a significant fate process.

Vapour phase photolysis under simulated sunlight did not occur after prolonged exposure (period not stated).

Experimental determination of its rate of reaction with hydroxyl radicals gave a half-life of >23 days. A computer estimate of its half-life due to H-atom abstraction by hydroxyl radical yields a calculated half-life of 7.12 days. Typically measured data are more reliable than

calculated data.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

25.10.2004 (53)

Type : air Light source :

Light spectrum: nm

Relative intensity: based on intensity of sunlight

Deg. product

Method Year GLP

Test substance : as prescribed by 1.1 - 1.4

ld 78-87-5 Date 14.12.2004

Remark

: I. Lifetime of 1,2-Dichloropropane

Rate of Reaction of 1,2-Dichloropropane with Hydroxyl Radical The absolute rate constant has been measured for the gas-phase reaction of hydroxyl radicals with 1.2-dichloropropane. Experiments were carried out using the pulsed laser photolysis-laser induced fluorescence technique over the temperature range 233-372 K. The kinetic data obtained were used to derive the following Arrhenius expression:

 $k=(2.1\pm0.5)x10-12 \exp[(453\pm76)/T]$ (in units of cm3molecule-1 s-1)

The quoted errors for the pre-exponential factor, A, and E/R are given by (delta)A=2Asigma(InA) and E/R=2sigma(E/R) respectively. At room temperature, the rate constant obtained is (4.6±0.6)x10-13 cm3molecule-1s-1.

OH + CH2(CI)CH(CI)CH3--> products

The rate constant obtained at 298 K was compared with the calculated one using a quantitative structure-activity relationship (QSAR.) The calculated value, 5.2 x10-13 cm3molecule-1s-1 was in excellent agreement with the experimental one.

Upper Limit on Rate of Reaction of 1,2 -Dichloropropane with Hydroxyl Radical

The rate constant for reaction of 1.2-dichloropropane with hydroxyl radical is <4.4x10-13cm3 molecule-1sec-1 at 296 K (23°C) based on its rate relative to dimethyl ether. That does not contradict the work above, since the discrepancy is well within the experimental error of the measurements.

Estimation of the Lifetime of 1,2-Dichloropropane

The lifetime (t=1/(k[OH]) of 1,2-dichloropropane, was estimated by using a global tropospheric 24-hour average OH radical concentration of 1x10⁶ molecule cm-3 and the measured bimolecular rate constant at room temperature. The tropospheric lifetime of 25 days is relatively short and hence one should consider the oxidation products to evaluate its atmospheric impact.

II. Products of Oxidation of 1,2-Dichloropropane

The QSAR for estimating the rate of reaction of 1,2-dichloropropane with hydroxyl radicals (3) also provides an estimate of the amount of hydrogen abstraction from each carbon atom; 60% from the central carbon, 29% from the chloromethyl (-CH2CI) group and 11% from the methyl group.

The products of chlorine-initiated oxidation of a similar molecule, 1,2,3trichloropropane have been studied. 1,2,3-Trichloropropane is oxidized through CICH2CCI(*)CH2CI and CICH2CHCICH(*)CI radicals which are analogous to the major radical products of H-abstraction from 1,2dichloropropane by HO*.

The initial radicals react with oxygen to form peroxy radicals (ROO*) which are reduced, largely by reaction with NO, to alkoxy radicals (RO*).

By analogy to the decomposition of CH2CICCI(O*)CH2CI, which yields a majority of 1,3-dichloroacetone by CI atom loss and some HC(=0)CI and CICH2C(=O)Cl by C-C bond cleavage followed by oxidation of CICH2*, the

ld 78-87-5 **Date** 14.12.2004

main products from 1,2-dichloropropane will be chloroacetone, acetyl chloride (CH3C(=O)Cl) and formyl chloride (HC(=O)Cl) as shown in the following reactions.

CH3CCI(O*)CH2CI CH3C(=O)CH2CI +CI*

CH3CCI(O*)CH2CI CH3C(=O) CI + *CH2CI

The minor attack at the CH2Cl group leads to an alkoxy radical that, by analogy to similar attack on 1,2,3-trichloropropane, will yield some CO2 and the CH3CHCl radical as well as uncertain amounts from other pathways leading ultimately to HCl and acetyl chloride.

CH3CHCICH(*)CI ---> CH3CHCICH(OO*)CI ---> CH3CHCICH(O*)CI

CH3CHCICH(O*)CI ---> CH3CHCIC(=O)* + HCI --> --> CH3CHCIC(=O)O*

CH3CHCIC(=0)O* ---> CO2 + CH3CH(*)Cl ---> ---> CH3C(=0)Cl or HCl + CH3C(=0)*

Fate of Oxidation Products

Chloroacetone

Chlorination of acetone results in a red shift and increase of the UV absorption. The UV spectrum of chloroacetone much more closely resembles that of 1,3-dichloroacetone than acetone. Using the actinic flux (the quantity of light available to molecules at a particular point in the atmosphere) representative of a summer day at 40° N the photolysis lifetime for 1,3-dichloroacetone is between 30 minutes and 12 hours. The estimated photolysis half-life of acetone is ~80 days at the surface and ~30 days at 5 km at 40° N in the summer. Thus the half life of chloroacetone will be much shorter than that required for transport to the stratosphere.

The estimated lifetime of chloroacetone due to reaction with hydroxyl radicals in the atmosphere is 29 days based on kOH= 0.3682 x 10-12 cm3 molecule-1 sec-1 and days with an average of 1 x 106 molecules cm-3 of HOo for 12 hours of daylight. Photolysis will be the main pathway of removal of chloroacetone from the atmosphere, but reaction with HOo also is sufficient to prevent significant transport of chlorine to the stratosphere.

HCl, Acetyl chloride (CH3C(=O)Cl) and Formyl chloride (HC(=O)Cl)

The atmospheric fate of these compounds is expected to be incorporation into rain-cloud-fog water followed by hydrolysis and removal by wet deposition within probably 5-15 days.

Similarly, HC(=O)Cl and CH2ClC(=O)Cl, the chlorinated organic products from photooxidation of 1,2-dichloroethane, are considered to have lifetimes in the lower atmosphere which are much shorter than that required for transport to the stratosphere and so are incapable of delivering significant amounts of chlorine to the stratosphere.

III. Ozone Depletion Potential of 1,2 Dichloropropane

Based on the lifetime and the products of oxidation, emission of 1,2-dichloropropane will not put a significant amount of chlorine into the

ld 78-87-5 **Date** 14.12.2004

stratosphere, and the ozone depleting potential of 1,2-dichloropropane is negligible.

IV. Global Warming Potential of 1,2 Dichloropropane

The tropospheric lifetime of 1,2-dichloropropane, based on its rate of reaction with hydroxyl radicals and the average tropospheric hydroxyl concentration, is 25 days. This is very short compared to the time horizons for global climate change.

A rough comparison to 1,1,1-trichloroethane, CH3CCl3,based on a comparison of lifetimes and infrared spectra, suggests that the GWP of 1,2-dichloropropane relative to CO2 will be 7 for a time horizon of 20 years and 2 for a time horizon of 100 years.

Thus, the global warming potential of 1,2-dichloropropane is negligible.

V. Photochemical Ozone Creation Potential (POCP) of 1,2 Dichloropropane

The potential of 1,2-dichloropropane to form ozone in polluted air, although not specifically determined, is clearly low. The POCP under the 5-day European base case is in the range of 2-25 compared to 100 for ethylene.

A rough estimate of the MIR (maximum incremental reativity) of 1,2-dichloropropane indicates that it is within a factor of two of that of ethane, which is considered to have "negligible photochemical reactivity" by the US

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Expert summary of available data.

Flag : Critical study for SIDS endpoint

25.10.2004 (54)

Type : air Light source :

Light spectrum : nm

Relative intensity: based on intensity of sunlight

INDIRECT PHOTOLYSIS

Sensitizer : OH

Conc. of sensitizer : 500000 molecule/cm³

Rate constant : <= .0000000000006 cm³/(molecule*sec)

Degradation : = 50 % after 27 day(s)

Deg. product

Method : other (calculated)

Year : 1984 **GLP** :

Test substance : no data

Remark: No catabolic products were found.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature: 22 degree C

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (55)

Type : air
Light source : nm

ld 78-87-5 **Date** 14.12.2004

Relative intensity

INDIRECT PHOTOLYSIS

based on intensity of sunlight

Sensitizer

Conc. of sensitizer : 500000 molecule/cm³

Rate constant : = .000000000016396 cm³/(molecule*sec)

Degradation : = 50 % after 10 day(s)

Deg. product

Method : other (calculated)

Year : 1987

GLP

Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium **Test condition** : The calculations refer to room temperature.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (56)

Type : air
Light source : Sun light
Light spectrum : nm

Relative intensity : based on intensity of sunlight

INDIRECT PHOTOLYSIS

Sensitizer : OH

Conc. of sensitizer : 2000000 molecule/cm³
Rate constant : cm³/(molecule*sec)

:

Degradation: % after

Deg. product

Method : other (calculated)

Year : 1982

GLP

Test substance : no data

Remark: The photochemical decrease of 1,2-dichloropropane was

laboratory tested. The decrease was calculated at 10.2 % per day with conditions of average temperature of 27 degrees

C and 12 hours of sunlight.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (57)

Type : air
Light source : Sun light
Light spectrum : nm

Relative intensity: based on intensity of sunlight

Remark: The direct photolysis of 1,2-dichloropropane is not relevant

in the troposphere, as 1,2-dichloropropane does not absorb

simulated sun light higher than 290 nm.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (58)

Type : other: Silica
Light source : Sun light
Light spectrum : nm

Relative intensity: based on intensity of sunlight

ld 78-87-5 **Date** 14.12.2004

Deg. product

Method : other (measured): Stability Test

Year : 1980 GLP : no data Test substance : no data

Remark : In presence of activated Silica the photomineralization of

1,2-dichloropropane was examined.

Activated Silica was exposed for 96 hours to a

Hg-high pressure lamp (simulated sun light Lambda > 290 nm)

through Pyrexglas. The determination of the photominerali zation was tracked by CO2 -formation. It was observed that the oxidative degradation (build of CO2 and CI-) of 1,2-dichloropropane which is adsorbed on the surface of the Silica, highly depends on the activation of the Silica (surface catalyzed photolysis). In non-activated Silica a buildup of 1.8 % CO2 and 3 % CI- was determined; in activated Silica buildup was 45.9 % CO2 and 60.7 % CI-. The activation highly influences the mineralization. This points to the fact that the photooxidative decrease of CO2 takes place at the surface and not in the gaseous phase. It is yet to be known if these lab results remain the same in

nature for 1,2-dichloropropane, which can adsorb to aerosol surfaces, dusts, sands etc.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (59)

Type : water

Light source

Light spectrum : nm

Relative intensity : based on intensity of sunlight

Deg. product

Method : other (measured): Stability Test

Year : 1988
GLP : no data
Test substance : no data

Remark: The catabolism of 1,2-dichloropropane has been tested in

Pyrex vessels containing demineralized water. As Pyrex absorbs wave-length < 290 nm, the sunlight spectrum of the troposphere was simulated during the irradiation. The transformation rate was 4 % after 180 minutes irradiation with 5.65 mg 1,2-dichloropropane/I starting concentration and was 8 % after 120 min irradiation with a starting concentration of 10.17 mg 1,2-dichloropropane/I. This results in the half-life times estimated at ca. 50.9 hours

and 16.6 hours.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (60)

Type : water
Light source : Xenon lamp
Light spectrum : = 450 nm

Relative intensity: based on intensity of sunlight

DIRECT PHOTOLYSIS

Halflife t1/2 : = 5.8 minute(s)

ld 78-87-5 **Date** 14.12.2004

Degradation : % after

Quantum yield : Deg. product :

Method : other (measured): Stability Test

Year : 1992 GLP : no data

Test substance : other TS: purity = 97 %

Remark: An unbuffered sample (with pH-values between 4.5

and 6.6) was irradiated using titandioxide (1 g/l) as a photo catalyst. To keep the titandioxide in solution, it was stirred with a magnetic stir. For control there was a solution without titandioxide kept in darkness.

The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (61)

3.1.2 STABILITY IN WATER

Source

Type : abiotic t1/2 pH4 : at °C

t1/2 pH7 : ca. 15.8 year at 25 °C **t1/2 pH9** : ca. 15.8 year at 25 °C : ca. 15.8 year at 25 °C

Deg. product
Method
Year
GLP

Test substance: as prescribed by 1.1 - 1.4

Remark: Calculated half-life of 15.8 years.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

25.10.2004 (33)

Type : abiotic t1/2 pH4 : at °C

t1/2 pH7 : ca. 283 month at 25 °C

t1/2 pH9 : at °C

Deg. product

Method : other: Stability Test

Year : 1988
GLP : no data
Test substance : no data

Remark: In sea water (at a pH-value of 8.3) the half-life time of

1,2-dichloropropane shortens to 60 months (5 years).
Hydrolysis produces 1-Chlor-2-propanol and HCI.
The 1,2-Dichloropropane ICCA/HPV Consortium

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : The tests were treated with demineralized water.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (60)

Type : abiotic **t1/2 pH4** : at °C

ld 78-87-5 **Date** 14.12.2004

t1/2 pH7 : at °C **t1/2 pH9** : at °C

Deg. product : Method : Year :

GLP : no data
Test substance : no data

Remark: The hydrolysis rate constant (KN) of 1,2-dichloropropane is

7.2 x 10E-4h-1 at 25 degrees C under natural conditions.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (47)

 Type
 : abiotic

 t1/2 pH4
 : at °C

 t1/2 pH7
 : at °C

 t1/2 pH9
 : at °C

Deg. product Method

Year

GLP : no data **Test substance** : no data

Remark: Under relevant conditions to the environment there was no

hydrolytical decrease established.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (62)

3.1.3 STABILITY IN SOIL

Type : laboratory

Radiolabel

Concentration

Soil temperature : °C Soil humidity :

Soil classification Year

Deg. product

Method : other: Dissipation Test

Year : 1974

GLP :

Test substance :

Remark: The half-life time was tested on an average of 2 sand

grounds (organic compounds 7.7% and 1.9%; pH value 4.3 and 5.0) and 2 clay grounds (organic compounds 1.5% and 1.8%; clay content 7.9% and 17.4%; pH value 7.7 and 7.6). The grounds were enriched with 1,2-dichloropropane in closed glass vessels (9 times bimonthly). Twenty-seven months after

the last addition of 1,2-dichloropropane the organic chloride content of the grounds was analyzed to determine the reduction of 1,2-dichloropropane. There was no control with contaminated or sterilized ground (only ground without

the 1,2-dichloropropane enrichment).

ld 78-87-5 **Date** 14.12.2004

Result: The following average h alf-life times were obtained:

Temp Half-life time (degrees C) (days)

2 74

15 52

20 41

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (63)

Type : other: soil-air (calcalation)

Radiolabel

Concentration

Soil temperature : °C Soil humidity :

Soil classification Year

Deg. product

Method

Year : 1976

GLP

Test substance :

Remark : 1,2-dichlorpropane was applied in open vessels that were

placed outside in a sandy-clay ground layer 3 cm thick, in

12 cm depth.

Result : 1,2-dichlorpropane evaporated by 99% in 10 days. Volatile

catabolic products could not be detected.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

25.10.2004 (64)

3.2.1 MONITORING DATA

Type of measurement: background concentration

Media: ground waterConcentration: $= .2 - 19.4 \mu g/l$

Method : Limit of detection = 0.2 ug/l

Remark: Samples of untreated ground water from 1,926 rural,

self-supplied domestic wells in the USA were analyzed for VOCs, including 1,2-dichloropropane, during 1986-1999. Reviewer's comment: this period covers the phase-out (1984-1989) and subsequent delisting of PDC as a soil fumigant in the USA, including a 10-yr follow-up period.

Data were complied from two sources:

* Samples analyzed by the USGS National Water-Quality Laboratory between 1993-1999 as part of the US Geological Survey's National Water-Quality Assessment Program. Samples were analyzed using purge and trap gas chromatography-mass spectrometry.

opoon on our

* Samples analysed as part of an ambient ground water/source water quality monitoring program conducted by local, State and other Federal agencies between 1986-1995. Analysis was

performed by a US-EPA certified laboratory (variety of

methodologies, not reported).

ld 78-87-5 Date 14.12.2004

Results from these analyses were included in the report only if the analytical limit of detection was 0.2 ug/l or less (i.e. 0.2 ppb or below).

PDC was present in 15/1926 samples at detected concentrations of 0.2-19.4 ug/l, with a median of 0.5 ug/l (500 ppt).

The analyzed concentration was greater than 5 ug/l in 2 of these 15 samples, and exceeded 10 ug/l in one of those 15, essentially 1 out of 1926 total samples analyzed.

Reviewer's comment: by inference, 13/15 of the 'positive' samples contained PDC at a concentration of 0.2-5 ug/l. The vast majority of samples (1911/1926 = 99.2%) contained no detectable PDC (at a limit of detection of 0.2 ug/l or 200

Source

The 1,2-Dichloropropane ICCA/HPV Consortium Conclusion 1.2-dichloropropane was present at concentrations of 0.2-19.4 ug/l in 15 of 1926 ground water sources from the USA analyzed during the period 1986-1999. Only two samples contained PDC at concentrations in excess of 5 ug/l. The vast majority of samples (1911/1926 = 99.2%) contained no

background concentration

detectable PDC (at a limit of detection of 0.2 ug/l).

Reliability (2) valid with restrictions

Monitoring studies conducted by US government agency

25.10.2004 (65)

Type of measurement

Media Concentration

Method Limit of detection at or below 2 ppt

Remark Measurements of urban air concentrations of 24 selected VOCs, including

> 1,2-dichloropropane, were conducted over periods of approx. 2 wk at 4 urban locations in the USA during the mid-1980s:

- San Jose, CA ("Silicon Valley"); April, August and December 1985 (total 35 days of sampling) - Downey, CA; February 1984 (total 10 d)

- Houston TX; March 1984 (total 9 d)

- Denver CO; March-April 1984 (total 8 d)

Air samples were collected using a stainless steel manifold, 5 m above ground level. In the majority of locations, samples were collected 3-5 min over 1-2 hr whereas a 2 hr integrated collection regime was employed at San Jose. On average 500 ml ambient air was collected at each location, cryoconcentrated (liquid argon) and analyzed immediately by electron capture detector GC. The analytical equipment was calibrated once or twice each day using appropriate concentration standards. External audit (Northrop Services Inc., under contract to US-EPA) indicated a precision of +/-15% and accuracy of +/-30%

Reviewer's comment: no limit of detection was given for PDC however, based on results obtained, this would appear to be 2 ppt or below.

The following arithmetic mean ambient air concentrations (ppt, parts per trillion; range in parenthesis) were

ld 78-87-5 **Date** 14.12.2004

reported:

San Jose, CA: 31 (9-70), 25 (9-61), 24 (9-35)

Downey, CA: 35 (<2-157) Houston TX: 158 (<2-724) Denver CO: 163 (<2-312)

Reviewer's comment: the authors do not discuss these findings, which were generally one order of magnitude below the analyzed concentration of other VOCs reported in this

study.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: The concentration of 1,2-dichloropropane in ambient air was

in a range <2-157 ppt at two locations in California, <2-312 ppt in Denver, CO and <2-724 ppt in Houston, TX. Arithmetic mean concentrations were consistently less than 1 ppb

(between 24 and 163 ppt).

Reliability : (2) valid with restrictions

Research investigation, suitable for assessment.

25.10.2004 (66)

Type of measurement: background concentration

Media : air Concentration : Method :

Remark: In 1980 1,2-dichloropropane measured a maximum concentration

of 6.93 ug/m3 taken in 350 samples from the air in

Terschelling Island, The Netherlands.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (67)

Type of measurement: background concentration

Media :
Concentration :
Method :

Remark: From February - April 1984 the average of 7 samples showed

0.03 ug 1,2-dichloropropane/m3 air (mimimum 0.02 ug, maximum

0.04ug) found in Portland, Oregon, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: < 0.02 ug/m3

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (68)

Type of measurement: background concentration

Media :
Concentration :
Method :

Remark : From 1970 - 1980 minimum 0.10 ug, maximum 0.52 ug and an

average of 0.27 ug 1,2-dichloropropane/m3 was found in 396 air samples in cities and suburbs in the USA. During the

same time minimum 0.006 ug, maximum 0.51 and an average 0.47 ug 1,2-dichloropropane was found in headwaters in the USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

ld 78-87-5 **Date** 14.12.2004

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (69)

Type of measurement: background concentration

Media :
Concentration :
Method :

Remark: 1,2-dichloropropane was qualitatively found in interior air

of a new office building in the USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (70)

Type of measurement: background concentration

Media : air Concentration :

Method

Remark : On March 29, 1982, 2.00 ug 1,2-dichloropropane/m3 was found

in the pristine continental troposphere in Gaulihuette near

Grindelwald, Switzerland. On April 1, 1982 1.90 ug

1,2-dichloropropane/m3 was found in Ankenbelli in the Swiss Alps. In June 1982, in the marine troposphere above the Azores, 1.9 - 7.0 ug 1,2-dichloropropane m/3 was found (n=5) and above Madeira 0.95 ug 1,2-dichloropropane/m3 was found

(n=4).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: < 0.85 ug/m3

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (71)

Type of measurement: background concentration

Media :
Concentration :
Method :

Remark : On March 14, 1991 analysis of the air in Rome tested 0.47 ug

1,2-dichloropropane m/3 air.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: 0.01 ug/m3

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (72)

Type of measurement: background concentration

Media : air Concentration : Method :

Remark : In July 1978 the atmosphere of nine apartment houses in "Old

Love Canal" (Niagara, New York, USA) were tested and two

cases of 1,2-dichloropropane were found.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

ld 78-87-5 **Date** 14.12.2004

reliability.

25.10.2004 (73)

Type of measurement: background concentration

Media : air Concentration :

Method :

Remark: From May 1980 - April 1981 in the cities of Houston, St.

Louis, Denver, Riverside, States Island, Pittsburgh and Chicago, an average between 0.11 and 0.38 ug 1,2-dichloropropane/m3 per location was found (9 - 10

samples/location).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (57)

Type of measurement: background concentration

Media : air Concentration :

Method :

Remark: On December 16, 1981 a single measure of 0.85 ug

1,2-dichloropropane/m3 air was found and on January 8, 1982 a single measure of 1.26 ug 1,2-dichloropropan/m3 air was found on the outskirts of Ulm, Germany. On May 25, 1982 the average of 2 measures showed concentrations of 1.70 ug 1,2-dichloropropane/m3 in the air. On June 25, 1982 a single measure showed 3.10 ug 1,2-dichloropropane/m3 in the city of Ulm. On February 26, 1982, 2 measures showed a concentration of 2.0 ug 1,2-dichloropropane/m3 in the unpolluted area from Weiherkopf near Sonthofen (pristine continental troposphere)

in the Allgaeuer Alps in Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Proof limit: < 0.85 ug/m3
Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (74)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark : From April 08 - 26, 1986 a concentration of < 2 ug/l

1,2-dichloropropane was found in the Potomac River

(Virginia, USA).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (75)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark: On October 29, 1981, traces of 1,2-dichloropropane were

ld 78-87-5 **Date** 14.12.2004

found in the wilderness of Lake Crawford (Canada).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (76)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark : From April - July 1989 in an agricultural area in Big Creek

near Ontario, Canada, 44 samples were taken in four locations, 11 samples at a time and no 1,2-dichloropropane

was found.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: 0.16 ug/l Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (77)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Source

Remark : From 1986 - 1989 an average of <= 1 ug of

1,2-dichloropropane was found in the upper, lower and middle

courses and tributaries of the Rhine River.
The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (78) (79) (80) (81)

Type of measurement: background concentration

Media : surface water

Concentration :

Method :

Remark: From November 8 - 22, 1988 Rhine River water in

Mainz/Wiesbaden, Germany was tested and no

1,2-dichloropropane was detected

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: 20 ug/l Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (82)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark: In the water of Lake Haringvliet near Stellendam, the

Netherlands, 1,2-dichloropropane/I was found on a monthly

average respectively:

-January - March 1991 - 0,2 mg -April - May 1991 - 0,3 mg

ld 78-87-5 **Date** 14.12.2004

-June - July 1991 - < 0,1 mg

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (83)

Type of measurement: background concentration

Media : surface water

Concentration :

Remark : In 1980 and 1981 concentrations of 1,2-dichloropropane lower

than 7 ug/l were found in the German rivers of Elbe, Ems, Leine and Weser. In 1982, concentrations of

1,2-dichloropropane remain the same in the Ems, Leine and Weser rivers. In 1982 concentrations of 1,2-dichloropropane between <7 ug/l and 87 ug/l were found in the Elbe River.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (84)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark: From June - October 1978, an average concentration of 0.1 -

1.0 ug/l 1,2-dichloropropane (detection frequency of 3 %) in the Rhine River near Maassluis, the Netherlands. From 1979 - 1982 the average concentration in this location was also 0.1 - 1.0 ug/l. In October 1978 an average of 3 ug/l 1,2-dichloropropane was found in the Rhine near Lobith

(detection frequency of 3 %).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (85) (86)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark : In 1988 and 1989 an average concentration of 0.1 ug/l

1,2-dichloropropane (corresponding to the maximum) was found

in the Rhine River near Hagestein, Germany. The 1,2-Dichloropropane ICCA/HPV Consortium

Source : The 1,2-Dichloropropane ICCA/HPV Co

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (87)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark: From November 1975 - January 1976 an average concentration

ld 78-87-5 **Date** 14.12.2004

of 0.04 ug/l 1,2-dichloropropane was found in the lower

Rhine River in Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not as signable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (88)

Type of measurement: background concentration

Media : surface water

Concentration Method

Remark : In 1986, 1987 and 1989 an average concentration of 1 ug/l

1,2-dichloropropane was found and in 1988 a measurement of 1.3 ug/l 1,2-dichloropropane was found in the Wupper River

in Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (78) (79) (80) (81)

Type of measurement: background concentration

Media : surface water

Concentration : Method :

Remark : From 1981 - 1982 an average concentration of < 0.15 ug/l

1,2-dichloropropane was found in the Elbe River near

Schnackenburg, Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (89)

Type of measurement: background concentration

Media : other: rain water

Concentration :

Method :

Remark : Rainwater in Portland Oregon, USA was tested and no

1,2-dichloropropane was found.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: There was no detection limit given.

The samples were collected during rainfall. The

concentrations have been determined at the same time in the

gaseous and aqueous phases.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (68)

Type of measurement: background concentration

Media : other: rain water

Concentration : Method :

Remark : On July 31, 1982, 86 samples of drained rainwater from 19

cities in the U.S. were taken from 11 rivers. The only location detecting 1,2-dichloropropane was in Eugene,

ld 78-87-5 Date 14.12.2004

Oregon where 3 ug were found.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition The proof frequency was 1 %.

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (90)

Type of measurement background concentration

Media other: sediment

Concentration Method

Remark In May - June 1980, sediment samples found 0.2 - 0.4 ug

> 1,2-dichloropropane/kg (related to wet weight, average of 5 samples or an unknown number of mixed samples) in the outlets of Lake Pontchartrain on the Mississippi River

(mouth of the Gulf of Mexico).

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (91)

Type of measurement background concentration

Media ground water

Concentration Method

Remark Between July 1985 and December 1986 in the ground water of

> flat-grounded wells in 206 agricultural areas in Germany, maximum of 5.1 ug 1,2-dichloropropane has been found (total

number of samples 1534).

The 1,2-Dichloropropane ICCA/HPV Consortium Source

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (13)

background concentration Type of measurement

Media ground water

Concentration

Method

Remark Between April - July 1989 1,2-dichloropropane was not found

> in 33 samples of spring water (11 samples each, taken in 3 places) of the drainage area of Big Creek, an agricultural

area in southwest Ontario, Canada).

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition Detection limit: 0.16 ug/l Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (77)

background concentration Type of measurement Media other: drinking water

Concentration

Method

Remark From November 1975 - January 1976, an average of 0.40 ug/l

1,2-dichloropropane was found in filtrate on the river banks

ld 78-87-5 **Date** 14.12.2004

of the lower Rhine River in Germany and the Rhine River

filtrate was measured 0.09 ug/l 1,2-dichloropropane. The 1,2-Dichloropropane ICCA/HPV Consortium

Source : The 1,2-Dichlorope Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (88)

Type of measurement : background concentration Media : other: drinking water

Concentration : Method :

Remark: From 1979 - 1982, < 0.1 ug 1,2-dichloropropane/l was found

in drinking water processed from Rhine River water in the

Netherlands.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (85)

Type of measurement : background concentration Media : other: drinking water

Concentration : Method :

Remark: A maximum of 0.96 ug 1,2-dichloropropane/l was found in

ground water used as drinking water in the USA (186 samples,

5 positive).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (92)

Type of measurement : background concentration

Media : other: drinking water

Concentration : Method :

Remark: From August - September 1979, a maximum of 1 ug

1,2-dichloropropane/I was found in drinking water samples

from waterworks in Canada.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (93)

Type of measurement : background concentration

Media : background concentration
other: drinking water

Concentration : Method :

Remark : On October 29, 1981, a maximum of 0.21 ug/l

1,2-dichloropropane was found in the drinking water of Port Robinson, Canada and on this same date it was found that the concentration of 1,2-dichloropropane was below the limit of

detection in the drinking water in Niagara Falls and

Burlington, Canada.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

ld 78-87-5 **Date** 14.12.2004

Test condition : LOD: 0.03 ug/l Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (76)

Type of measurement : background concentration
Media : other: drinking water

Concentration : Method :

Remark : In July 1978, maximum 1.2 ug/l 1,2-dichloropropane was found

(lowest measured concentration) in 1 of 9 drinking water samples tested in Love Canal, Niagara Falls, New York, USA. From 1964 - 1979, trace levels of 1,2-dichloropropane were found in 14 drinking water samples in Niagara Falls and

Buffalo, New York, USA.(7 % positive samples)

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (73) (94)

Type of measurement: background concentration

Media : biota

Concentration : Method :

Remark: It is expected that a person of 70 kg absorbed 18.5 ug

1,2-dichloropropane/day in 1980 in the Netherlands, assuming a tidal volume of 20 m3/day and an absorption rate of 50 %.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (67)

Type of measurement: background concentration

Media : biota

Concentration : Method :

inetriod .

Remark: Blood samples tested in 22 people found 0.51 ug

1,2-dichloropropane/l of blood (n=4).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : LOD: < 0.05 ug/l **Reliability** : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (95)

Type of measurement: background concentration

Media : biota

Concentration : Method :

Remark: Human hair showed qualitative absorption of 1,2-dichloro-

propane.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Number of samples, locality and period of analysis: no

information

LOD: no information

ld 78-87-5 **Date** 14.12.2004

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (96)

Type of measurement: background concentration

Media : biota

Concentration : Method :

Remark: From May - June 1980, 1,2-dichloropropane was not found in

samples of oyster and mussels (average of 5 samples and mixed samples) from drains in Lake Pontchartrain (mouth of

Mississippi and Gulf of Mexico).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Proof limit: no information

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (91)

Type of measurement: background concentration

Media : food

Concentration : Method :

Remark: 1,2-dichloropropane was not found in milk and milk products

tested in the Netherlands (number of samples not given).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : LOD: no information

period of analysis: no information

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (97)

Type of measurement: background concentration

Media : food

Concentration : Method :

Remark : 1,2-dichloropropane was not found in 231 food stuffs tested

(probably in the area of Kansas City, Missouri, USA).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Proof limit: no information

period of analysis: no information

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (98)

Type of measurement: concentration at contaminated site

Media : air
Concentration :
Method :

Remark : In 1986 - 1987, concentrations of 1 - 198 ug/m3

1,2-dichloropropane were found in 9 locations in ground air above a disorganized dump (approximately 12 years old). The dump was located on top of a former brick factory where special and domestic waste was stored until 1974. From 1975 - 1978 the dump was filled with earth and rubble and in 1983

ld 78-87-5 **Date** 14.12.2004

it was partially cultivated.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (99)

Type of measurement: concentration at contaminated site

Media : air Concentration : Method :

Remark : From April 1986 - April 1987, 0.9 - 2.0 ug 1,2-dichloro-

propane/m3 air was found in 5 districts with large volumes of traffic (19000-72000 cars/day) in Hamburg, Germany. The annual average of 0.19 - 1.6 ug 1,2-dichloropropane/m3 was

measured in industrial areas.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (100)

Type of measurement: concentration at contaminated site

Media : air
Concentration :
Method :

Remark : In 1980, a maximum of 7.1 - 14.1 ug/m3 1,2-dichloropropane

was found in the industrial areas of the cities of Delft and

Vlaardingen, the Netherlands. On the average,

1,2-dichloropropane measured 0.28 - 0.65 ug/m3 (350

samples/location).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (67)

Type of measurement: concentration at contaminated site

Media : Concentration : Method :

Remark : In 1983/84, 1.20 ug 1,2-dichloropropane was measured in the

air (average from 310 samples in 10 localities) of the

industrial city of Philadelphia, PA, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (101)

Type of measurement: concentration at contaminated site

Media : air
Concentration :
Method :

Remark : In March 1980, 1,2-dichloropropane was found lower than the

proof limit in the industrial area (oil factory) of

Beaumont, Texas, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

ld 78-87-5 **Date** 14.12.2004

Test condition: Detection limit: 0.20 ug/m3

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (102)

Type of measurement : concentration at contaminated site

Media : air

Media :
Concentration :
Method :

Remark : From January - February 1977, 0.2 ug 1,2-dichloropropane/m3

was found in the chemical/industrial area of Iberville Parish, Louisiana, USA (11 samples, 6 positive).

In February 1978, 1.4 ug/m3 1,2-dichloropropane was found in the air of 1 in 6 cellars tested in apartment houses near a

dump in Niagara Falls, New York, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (103)

Type of measurement: concentration at contaminated site

Media : air
Concentration :
Method :

Remark : From 1964 - 1979 traces of 1,2-dichloropropane were found

in the industrial area of Niagara Falls, New York, USA (9 samples, 22 % positive). In the same time, a maximum of 3.999 ug 1,2-dichloropropane/m3 was found in the industrial areas of Baton Rouge, Louisiana, USA (39 samples, 38 %

positive).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (94)

Type of measurement: concentration at contaminated site

Media : a
Concentration :
Method :

Remark : From 1983 - 1988, 4 - 198 ug 1,2-dichloropropane/m3 was

found in the gas of an industrial sludge dump in

Bielefeld-Brake, Germany.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (104)

Type of measurement: concentration at contaminated site

Media : surface water

Concentration : Method :

Remark: Between September 22, 1981 and November 16-22, 1981, 0.22

- 0.44 ug/l of 1,2-dichloropropane was found in 5 of 82 measurements in Lake Ontario, Canada, contaminated

ld 78-87-5 **Date** 14.12.2004

by industrial and communal affluents. In 41 of these measurements, 1,2-dichloropropane was lower than the detection limit. On September 22, 1981, 0.01 - 0.055 ug/l 1,2-dichloropropane was found in 9 of 17 industrial areas

tested on the Niagara River in Canada.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Detection limit: 0.02 ug/l Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (105)

Type of measurement: concentration at contaminated site

Media : surface water

Concentration : Method :

Remark: In February 1976, > 1 ug/l 1,2-dichloropropane was found

from 30 samples taken in the longitudinal profile of the

communal and industrial areas surrounding the Delaware River

in the USA (detection frequency of 10 %).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (106)

Type of measurement: concentration at contaminated site

Media : ground water

Concentration : Method :

Remark: In 1988 in the Netherlands, after applying 170 kg

1,3-dichloropropane (containing 0.85 kg

1,2-dichloropropane)/ha, 0.1-200 ug 1,2-dichloropropane/l was found in 15 of 22 ground water samples of sand grounds

containing arable land for growing potatoes. In the remaining 7 samples, 1,2-dichloropropane concentrations were lower than the proof limit. After treating sand grounds growing flower bulbs (containing humus), with 600 kg 1,3-dichloropropane (containing 3 kg 1,2-dichloropropane)/ha, 6 of 8 ground water samples

showed 1-14 ug 1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Proof limit: 0.1 ug/l

Ground water 6 meters deep in an agricultural used area was analyzed. The area was treated with 1,3-dichloropropane, which contained until 1983 34 % of 1,2-dichloropropane; from

1984, it contained 0.5 %.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (107)

Type of measurement: concentration at contaminated site

Media : ground water

Concentration :

Remark : A concentration of > 100 ug/l 1,2-dichloropropane was found

in ground water at Suffolk County, New York, USA after the use of Telone (a mixture of 1,3-dichloropropane and

ld 78-87-5 Date 14.12.2004

1,2-dichloropropane).

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

(108)25.10.2004

Type of measurement

concentration at contaminated site ground water

Media Concentration

Method

Remark In April 1978, a concentration of 10 ug/l

> 1,2-dichloropropane was found in the ground water after 1,3-dichloropropane (Telone II, 92 %, application amount 140 l/ha) was used as a ground fumigate for 83 and 104 days and 6 ug/l 1,2-dichloropropane was found after 138 days of use. In October 1978, 5 ug 1,2-dichloropropane/I was found

in Suffolk County, New York, USA.

The 1,2-Dichloropropane ICCA/HPV Consortium Source

Test condition The fumigate was applied in 8-12 cm depth of ground in a

mud floor or clay-mud floor with sand and gravel drainage.

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (109)

Type of measurement concentration at contaminated site

Media around water

Concentration Method :

Remark : 1 - 50 ug 1,2-dichloropropane was found after

1,2-dichloropropane was used as a nematicide on surfaces of

4 states in the USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (11)

Type of measurement concentration at contaminated site

Media ground water

Concentration :

Method

Remark : A maximum of 1200 ug 1,2 -dichloropropane/I was found after

1,2-dichloropropane was used as a pesticide in 75 wells in

9 locations in California, USA.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (10)

concentration at contaminated site Type of measurement

Media ground water

Concentration

Method

Remark 1,2-dichloropropane was found in well water 30 m deep under

a factory producing colors.

ld 78-87-5 **Date** 14.12.2004

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Country and period of analysis: no information

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (110)

Type of measurement: concentration at contaminated site

Media : ground water

Concentration :

Method :

Remark : In May 1988, 3.2 - 11.0 ug 1,2 - dichloropropane/l was found

in the aquifer near a dump close to Ottawa, Ontario, Canada.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (111)

Type of measurement: concentration at contaminated site

Media : ground water

Concentration : Method :

Remark : 0.5 - 43 ug 1,2-dichloropropane/l was found in 8 in 13

ground water samples under dumps in Minnesota, USA. Also 1.1 ug 1,2-dichloropropane/l was found under a second urban

dump.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (112)

Type of measurement: concentration at contaminated site

Media : other: drinking water

Concentration : Method :

Remark : In September/November 1987, maximum 19.0 ug/l, minimum

0.7 ug/l (average 4.6 ug/l) was found in all 8 drinking water samples tested in East Windsor, Suffield and Bolton, USA after 1,2-dichloropropane containing pesticide was used. An average of 10 ug 1,2-dichloropropane/l was found in 12

wells of which drinking water was taken after

1,2-dichloropropane containing pesticides was used in the

USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (10) (113)

Type of measurement: concentration at contaminated site

Media : other: leachate

Concentration :

Remark: Samples in 3 places were tested after domestic and

industrial wastewater was brought in a dump in the USA. These 3 samples contained < 10 ug 1,2-dichloropropane/l in

ld 78-87-5 **Date** 14.12.2004

the water leakage. Two other places showed 18 and 37 ug

1,2-dichloropropane/l in the water leakage.
The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (114)

Type of measurement: concentration at contaminated site

Media : other: leachate

Concentration :

Source

Remark : 2.0 - 81 ug 1,2-dichloropropane/l was found in the dump

water leakage of 3 official communal dumps of which some

industrial waste was deposited in Minnesota, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (112)

Type of measurement: concentration at contaminated site

Media : biota

Concentration : Method :

Remark: 1,2-dichloropropane was not detected after samples of

exhaled air, urine and blood were taken from 9 persons in early July 1979 in the Love Canal dump area in Niagara

Falls, New York, USA.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (73)

Type of measurement: concentration at contaminated site

Media : biota Concentration :

Method :

Remark: The usual amount of 1,3-dichloropropane-1,2-dichloropropane

mixture (D-D-mixture, containing 23 % 1,2-dichloropropane) labeled radioactive, was used and potatoes were planted 5

months after ground treatment.

At the time of planting, ground radioactivity was estimated at 5 - 10 % of the applied radioactivity. Four months later the potatoes were gathered and the radioactivity was 5 % of the applied amount. 0.007 mg 1,2-dichloropropane/kg was

found in the potatoes.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (64)

Type of measurement: concentration at contaminated site

Media : ground water

Concentration : Method :

ld 78-87-5 Date 14.12.2004

Remark : In April/May 1978, no 1,2-dichloropropanewas found inwell

> water tested on days 10, 13, 26 and 49, after adding 80 ml/m2 of the pesticide Ditrapex, containing 24 %

1,2-dichloropropane. The pesticide was administered at 25 cm to ground covered with foil in the greenhouses. In the same time period, 130 ug 1,2-dichloropropane/l was found on day 10 after adding 75 ml Ditrapex/m2 to drainage water.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition Detection limit: 5,78 ug/l Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

25.10.2004 (14)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

fugacity model level I Type

Media

Air 98.02 % (Fugacity Model Level I) Water : 1.82 % (Fugacity Model Level I) Soil .16 % (Fugacity Model Level I) Biota % (Fugacity Model Level II/III) Soil % (Fugacity Model Level II/III)

Method Year

Method Input Parameters:

Molecular Mass (g/mol): 112.99

Temperature (°C): 20

Loa Kow: 2.0

Water Solubility (g/m3): 2800 Vapor Pressure (Pa): 6620 Melting Point (°C): -100.4

Fugacity ratio: 1.0

Result Distribution of PDC in the environment based on Level I

model:

Compartment Distribution (Percent)

98.02 Air Water 1.82 0.16 Soil Biota (fish) < 0.01 Suspended Sediment < 0.01 Bottom Sediment < 0.01

The 1,2-Dichloropropane ICCA/HPV Consortium Source

Reliability (2) valid with restrictions

Accepted computational method.

Critical study for SIDS endpoint Flag

25.10.2004 (33)(115)

Type fugacity model level III

Media

Δir 98.85 % (Fugacity Model Level I) Water : .93 % (Fugacity Model Level I) Soil .21 % (Fugacity Model Level I) **Biota** % (Fugacity Model Level II/III)

ld 78-87-5 Date 14.12.2004

Soil % (Fugacity Model Level II/III)

Method Year

Method Input Parameters for Level III:

Molecular Mass (g/mol): 112.99

Temperature (°C): 20

Loa Kow: 2.0

Water Solubility (g/m3): 2800 Vapor Pressure (Pa): 6620 Melting Point (°C): -100.4 Fugacity ratio: 1.0

Reaction Half-lives (hr)

Air: 550 Water: 550 Soil: 1700 Sediment: 5500

Level III Emissions: 1,000 kg/hr to air only.

According to U.S. EPA TRI Database, >99.9% of reported PDC

emissions are to the atmosphere.

Result Distribution of PDC in the environment based on Level III

model:

Compartment Distribution (%) Concentration (µg/m3)

Air 98.85 0.89 Water 0.93 4.2

Soil 0.21 10

Sediment < 0.01

Advection in air accounts for 88.6% of removal rate

Reaction in air accounts for 11.2% of removal rate

Advection and reaction in water, sediment, and soil account

of 0.2% of removal rate

The 1,2-Dichloropropane ICCA/HPV Consortium Source Level I and III models predict that PDC will be Conclusion

predominately transported to the atmosphere, with little or no potential for deposition to soil and water. Advection is the predominant removal mechanism in the atmosphere.

Reliability (2) valid with restrictions

Accepted computational method.

Critical study for SIDS endpoint Flag

25.10.2004 (33)(115)

Type adsorption Media water - soil

Air % (Fugacity Model Level I) Water % (Fugacity Model Level I) Soil % (Fugacity Model Level I) Biota % (Fugacity Model Level II/III) Soil % (Fugacity Model Level II/III)

Method other: Calculation

Year 1980

Result For 1,2-dichloropropane, a ground sorption coefficient Koc

299.14 can be calculated on a basis of n-Octanol/water partition coefficient log Pow 2.02 according to the

formula of Kenaga and Goring (1980) log Koc = 1.377 + 0.544

(log Pow).

ld 78-87-5 **Date** 14.12.2004

Therefore, according to Blume (1990) low ground sorption is

expected.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Data from a handbook

25.10.2004 (116) (117)

Type : adsorption Media : water - soil

 Air
 : % (Fugacity Model Level I)

 Water
 : % (Fugacity Model Level I)

 Soil
 : % (Fugacity Model Level I)

 Biota
 : % (Fugacity Model Level II/III)

 Soil
 : % (Fugacity Model Level II/III)

Method : other: Calculation

Year : 1982

Result : A ground sorption coefficient of 50 was calculated on the

basis of the n-Octanol/water partition coefficient Pow 105

according to the formula Koc - 0.48 x Pow.

According to Blume (1990) the expectation is from very low

to low ground sorption.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions
Data from a handbook

25.10.2004 (116) (47)

3.3.2 DISTRIBUTION

Media : other: static distribution in air - biota - sediment(s) - soil - water

Method : Calculation according Mackay, Level I

Year : 2003

Result : Compartment Level I amount, %

Air 98.0 Water 1.82 Soil 0.161

Sediment 3.6E-03

Suspended particles 1.1E-04

Fish 9.1E-06

Conclusion : In a static fugacity-driven distribution model without advection or reaction,

1,2-dichloropropane is expected to distribute mainly to air (98 %) with water (1.8 %), soil (0.16%), sediment (3.6E-03%), suspended particles (1.1E-04%) and fish (9.1E-06%) being serially less important compartments.

Reliability : (2) valid with restrictions

Widely used and accepted computer distribution model, reliability 2.

Flag : Critical study for SIDS endpoint

12.10.2004 (118)

Media : other: dynamic distribution in air - biota - sediment(s) - soil - water

Method : Calculation according Mackay, Level III

Year : 2003

Result : Dynamic distribution, Level III amount, %

Emissions, kg/h, to air water soil sediment

3000 0 0 0

Compartment Air 98.5 Water 1.3 Soil 0.2

Id 78-87-5 Date 14.12.2004

5.3E-03 Sediment Residence time, h 90.9

> 0 3000 0 0

Compartment Air 16.9 Water 82.7 Soil 0.04 Sediment

Residence time, h 369

0 3000 0

0.34

Compartment Air 41.3 Water 3.7 55.0 Soil

Sediment 0.015

Residence time, h 216

Model conditions

degradation rates (Half-lives): air = 600 h; water, soil, sediment = 1.0E11 h (negligible). Data temperature = 25°C; water solubility = 2800 mg/l, vapour

pressure = 6620 Pa; $\log \text{Kow} = 2.00$; melting point = -100.4°C.

Conclusion The Level III dynamic distribution model highlights the importance of the

> emission pathway. For realistic emissions only to air, the main distribution is expected to air (98.5%) and secondarily to water (1.3%) and soil (0.2%), while sediment (5.3E-03%), suspended particles (7.9E-05%) and fish

(6.4E-06%) are unimportant.

(2) valid with restrictions Reliability

Widely used and accepted computer distribution model,

reliability 2.

Critical study for SIDS endpoint Flag

12.10.2004 (119)

Media other: NaCI - air Method other (measurement)

Year 1989

Result : A partition coefficient of 2.75 for 1,2-dichloropropane

in 0.9% NaCl/air was calculated at a temperature of 37

degrees C.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (120)

Media other: olive oil - air Method other (measurement)

Year 1979

Result : A partition coefficient of 747 and 428 for

1,2-dichloropropane in olive oil/air was calculated at 37

degrees C.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (121)

Media other: olive oil - blood Method other (calculation)

ld 78-87-5 **Date** 14.12.2004

Year : 1979

Result: A partition coefficient of 70 for 1,2-dichloropropane in

olive oil/blood was calculated at 37 degrees C.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (121)

Media: other: olive oil - waterMethod: other (calculation)

Year : 1979

Result : A partition coefficient of 138 for 1,2-dichloropropane in

olive oil/water was calculated at 37 degrees C.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (121)

Media: other: organic matter - airMethod: other (calculation)

Year : 1980

Remark: The partition coefficient between the organic and gaseous

phase (Kom/g) was calculated.

Result: The partition coefficient Kom/g is:

at 15 degrees C 134 ug/g organic dry mass x (ug/ml gas)-1 at 20 degrees C 118 ug/g organic dry mass x (ug/ml gas)-1 at 29 degrees C 79 ug/g organic dry mass x (ug/ml gas)-1

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (63)

Media : other: organic matter - water

Method : other (calculation)

Year : 1980

Remark : The partition coefficient between the organic and water

phase (Kom/w) was calculated.

Result : The partition coefficient Kom/w at 15, 20 and 29 degrees C

is 11 ug/g dry mass x (ug/ml water)-1.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (63)

Media: water - airMethod: other (calculation)

Year : 1984

Remark: The calculated Henry constant is 212.78 Pa x m3 x mol-1 at

20 degrees C.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

ld 78-87-5 **Date** 14.12.2004

26.10.2004 (122)

Media : water - air

Method : other (measurement)

Year

Remark : A Henry constant at 20 degrees C for 1,2-dichloropropane was

calculated at 192.52 - 273.51 Pa x m3 x mol-1 and at 25

degrees C, at 361.73 Pa x m3 x mol-1.

According to Thomas (1982) as 1,2-dichlorpropane is a light volatile substance, a transition from aqueous solution of 1,2-dichloropropane evaporates in the atmosphere.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (123) (45)

Media : water - air

Method : other (measurement)

Year : 1980

Remark: A water solution, enriched with 1 mg 1,2-dichlorpropane/l,

had a high of 1,6 cm. It was stirred at 24 degrees C with a

magnetic stirrer at 100 +/- 10 U/min.

Result : In a simulation experiment 1,2-dichloropropane was de-gassed

out of an aqueous solution in the laboratory and after 8

minutes it had evaporated by 50 %.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (124)

Media : water - air

Method : other (measurement)

Year : 1984

Result : A relative transfer coefficient of 0.57 for

1,2-dichloropropane was determined in a laboratory experiment in a circulating current (speed 1 m x s-1, 1 m depth). Based on this coefficient, the half-life time for the evaporation of 1,2-dichloropropane was approximately 6

hours.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (125)

Media : water - air

Method : other (measurement)

Year : 1984

Result : The Henry constant in a closed system calculated at 10

degrees C 124 Pa x m3 x mol-1, at 15 degrees C 128 Pa x m3 x

mol-1, at 25 degrees C 362 Pa x m3 x mol-1 and at 30

degrees C 290 Pa x m3 x mol-1.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

ld 78-87-5 **Date** 14.12.2004

26.10.2004 (123)

Media : water - air

Method : other (measurement)

Year : 1979

Result: An 8-hour volatility laboratory experiment in a

"wind-wave-tank" resulted in a Henry-constant calculated as

274 Pa x m3 x mol-1 at 20 degrees C . A general

liquid-mass- transfer-coefficient KOL of 28.9 - 93.9 x 10E6 m x s-1 was determined at wind speeds of 5.96 - 13.2 m x

s-1.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (45)

Media: water - airMethod: other (calculation)

Year : 1984

Remark : The diffusion loss from the water surface was < 5 - 10 %.
Result : A Henry constant of 213 Pa x m3 x mol-1 at 20 degrees C was

calculated.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (122)

Media : water - air

Method : other (measurement)

Year : 1975

Remark: The de-gassing was calculated in a simulation experiment

(stirred with a propeller, temperature: 25 degrees C, 200

rotations/minute).

Result : Dilling et al. (1975) made tests on other chlorinated

hydrocarbons. Relating to these tests the half-life time of evaporation of 1,2-dichloropropane out of water is \ll 50

minutes. The half-life time of evaporation of

1,2-dichloropropane out of water can differ from one to several hours depending on environmental conditions.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (62)

Media : water - air

Method : other (measurement)

Year : 1979

Result: The partition coefficient of 1,2-dichloropropane

water/air is 5.4 at a temperature of 37 degrees C.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (121)

ld 78-87-5 **Date** 14.12.2004

Media: water - airMethod: other (calculation)

Year : 1980

Remark: The partition coefficient between water and gaseous phase

(Kw/g) was calculated.

Result: The partition coefficient Kw/g is

at 15 degrees C 13 ug/ml water x (ug/ml gas)-1 at 20 degrees C 11 ug/ml water x (ug/ml gas)-1 at 29 degrees C 7 ug/ml water x (ug/ml gas)-1 The 12-Dichloropropage ICCA/HPV/Consortium

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (63)

Media : water - soil

Method : other (measurement)

Year : 1980

Remark : A measurement of 75 ml Ditrapex/m2, which contains 24 %

1,2-dichloropropane, was brought in through closed

lysimeter (cross-section 12 cm) 1.25 m long, 25 cm deep.

Result : During 26 days of 1600 mm precipitation, 1.43 % of the total

amount of applied 1,2-dichloropropane was found in water

leakage.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (14)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic

Inoculum: activated sludge, industrial, non-adaptedConcentration: 150 mg/l related to Test substance

related to

Result : under test conditions no biodegradation observed

Deg. product :

Method : OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens

Test"

Year : 2002 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Reaction mixtures were prepared by adding 150 mg/L PDC

directly to activated sludge (1,000 mg/L mixed liquor suspended solids) in a defined mineral medium. The test vessels were sealed to minimize the loss of PDC due to volatilization. Oxygen concentrations in the headspace of the vessels were monitored and oxygen gas was added as necessary to ensure that aerobic conditions were maintained.

ld 78-87-5 **Date** 14.12.2004

Abiotic control mixtures were prepared by adding PDC to activated sludge inhibited with mercuric chloride. Positive control mixtures were prepared with aniline added to activated sludge to confirm the viability of the microbial inoculum. Toxicity controls were prepared with aniline and PDC in activated sludge to determine if the test compound was inhibitory to the microbiol inoculum. The reaction mixtures were continuously mixed and incubated at 22 \pm 1 $^{\circ}$ C for 28 days.

Reaction mixtures were sampled after 0, 1, 2, 7, 14, 21, and 28 days to measure PDC and dissolved organic carbon (DOC) concentrations remaining in the mixtures. PDC concentrations in the reaction mixtures were determined by gas chromatography with flame ionization detection (GC-FID). Removal of aniline was determined by dissolved organic carbon (DOC) analyses of the reaction mixtures.

PDC and DOC concentrations were reported as the arithmetic mean of analyses from duplicate reaction mixtures.

 No biodegradation of PDC was observed in the test. No difference was observed in loss of PDC in viable mixtures

compared to abiotic controls over 28 days.

Aniline (reference compound) was extensively degraded in positive control mixtures (96% in 14 days), thereby confirming the viability of the microbial inoculum.

Extensive degradation of aniline in toxicity control

mixtures containing PDC (98% in 14 days) showed that PDC was

not inhibitory to the inoculum under the test conditions.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : PDC did not meet the criteria of inherent biodegradability

under the conditions of a modified OECD Method 302B test.

Reliability : (1) valid without restriction

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (126)

Type : aerobic Inoculum : activated sludge

Concentration: 1 mg/l related to Test substance

related to

Contact time

Result

Degradation: = 0 (\pm) % after 28 day(s)Result: other: not readily biodegradable

Deg. product

Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"

Year : 1981 GLP : no data

Test substance : other TS: purity = 65 %

Remark : A mixture with the main component 1,2-dichloropropane was

analyzed. Other compounds of the mixture were:

1,3-dichloropropene 25 % 2,3-dichloropropene 10 % 1,1-dichloropropane trace 3,3-dichloropropene trace

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature: 21 degrees C

Reliability : (4) not assignable

ld 78-87-5 **Date** 14.12.2004

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (127)

Type : aerobic

Inoculum : other: BASF-activated sludge

Concentration: mg/l related to DOC (Dissolved Organic Carbon)

related to

Contact time

Degradation : = 96 (±) % after 3 hour(s)

Result : other

Deg. product

Method : OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens

Test"

Year :

GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Remark: No conclusion can be made about biodegradation from this

study because of the high volatility of 1,2-dichloropropane.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (128)

Type : aerobic

 Inoculum
 : Nitrosomonas sp. (Bacteria)

 Concentration
 : .048 mg/l related to Test substance

related to

Contact time

Degradation: = 75 (±) % after 1 hour(s)Result: other: biodegradable

Deg. product

Method : other: Biodegradation Test

Year : 1990 GLP : no data Test substance : no data

Remark: Bacterial suspensions of bacteria living in the ground were

analyzed and no degradation products were given.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : pH-value: 7.7 **Reliability** : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (129)

Type : aerobic

Inoculum: Pseudomonas fluorescens (Bacteria)Concentration: 100 mg/l related to Test substance

related to

Contact time

Degradation : = 3 (±) % after 24 hour(s)

Result

Deg. product

Method : other: Biodegradation Test

Year : 1988 GLP : no data Test substance : no data

Remark: A decrease of 1,2-dichloropropane caused by an isolated

ld 78-87-5 **Date** 14.12.2004

bacterium from enriched water and ground samples from a contaminated industrial dump with 1,2 -dichloroethane and

1,2-dichloropropane was tested. This bacteria in

mineral-salt medium uses 1,2-dichloropropane. The carbon and energy sources, glucose (0.5 %) and yeast extract (0.005 %),

were added to the starting concentration of

1,2-dichloropropane. The decrease of 1,2-dichloropropane concentration in the medium was the measured parameter. The $\,$

microbial decrease was given in average of 3 samples.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : In order to record the microbial decrease of

1,2-dichlorpropane, it was incubated in a shaker at 25

degrees C.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (130)

Type : aerobic

 Inoculum
 : other: Nitrosolobus multiformis

 Concentration
 : .048 mg/l related to Test substance

related to

Contact time :

Degradation : = $40 (\pm) \%$ after 1 hour(s)

Result :

Deg. product

Method : other: Biodegradation Test

Year : 1990
GLP : no data
Test substance : no data

Remark : Bacterial suspensions (living bacteria in the ground) were

analyzed after the addition of 1 mM NH4CI.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : pH-value: 7.7 **Reliability** : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (129)

Type : aerobic

Inoculum : other: influent and effluent of chemical industrial waste water

Concentration: 182 mg/l related to Test substance

related to

Deg. product

Method : other: Biodegradation Test

Year : 1983 GLP : no data Test substance : no data

Remark: The elimination of 98.9 - 99.2 % according to the

1,2-dichlorpropane concentration in the drain was attributed

to the stripping.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition : The analysis took place in a 31 sludge reactor.

The "entering concentrations" of 1,2-dichlorpropane were

established after 5 days.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (131) (132)

ld 78-87-5 **Date** 14.12.2004

Type : aerobic

Inoculum : other: effluent from a university sewage treatment plant

Concentration: 70 mg/l related to Test substance

related to

Deg. product

Method : other: Filtration Test

Year : 1981 GLP : no data Test substance : no data

Remark : The decrease of 1,2-dichloropropane was tested on a pilot

machine using the meadow filtration method. Grass was planted on the filtration area (ground temperature was 20 - 22 degrees C). For 2 months before testing, they brought in the effluent sewage from a university. The established 1,2-dichloropropane elimination was 74 %. The question remains if 1,2-dichloropropane was eliminated through evaporation or from a biological decrease. In a "Leaching test" only "non-spiked" waste water was used. One day after the "Leaching test" began 1,2-dichloropropane was no longer

found in the water samples along the filtration

installation. We can conclude that a reversal adsorption did

not take place.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature of the waste water: 25- 29 degrees C,

Waste water rush rate: 0.17 m3/m x hour

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (133)

Type : aerobic

Inoculum: other: domestic waste water, adaptedConcentration: 10 mg/l related to Test substance

related to

Contact time

Degradation : = 81 (±) % after 7 day(s)

Result

Deg. product

Method: other: Flask-screening procedure of Bunch and Chambers

Year : 1967
GLP : no data
Test substance : no data

Remark: Evaporation of 3 %. This analysis is non-reliable due to

insufficient controls.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition : closed statistical test at 25 degrees C in dark

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (134)

Type : aerobic

Inoculum: other: domestic waste water, adaptedConcentration: 5 mg/l related to Test substance

related to

Contact time

Degradation : = 89 (±) % after 7 day(s)

Result :

Deg. product :

Method : other: Flask-screening procedure of Bunch and Chambers

ld 78-87-5 **Date** 14.12.2004

Year : 1967
GLP : no data
Test substance : no data

Remark: Evaporation of 3 %. This analysis is non-reliable due to

insufficient controls.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : closed statistical test at 25 degrees C in darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (134)

Type : aerobic

Inoculum : other: domestic waste water, non adapted

Concentration : 10 mg/l related to Test substance

related to

Contact time

Degradation : = 42 (±) % after 7 day(s)

Result

Deg. product

Method : other: Flask-screening procedure of Bunch and Chambers

Year : 1987 GLP : no data Test substance : no data

Remark : This analysis is unreliable due to insufficient controls.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (134)

Type : aerobic

Inoculum: other: BASF-activated sludgeConcentration: mg/l related to Test substance

related to

Contact time

Degradation : = 0 (±) % after 7 day(s)

Result : other

Deg. product

Method : other: not specified

Year

GLP : no data

Test substance

Remark: No additional information is provided.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (135)

Type : anaerobic

Inoculum : other: medium loam

Concentration : 71 mg/l related to Test substance

related to

Contact time :

Degradation : $=29 \pm 0.00$ (±) % after 140 day(s)

Result :

Deg. product

Method : other: Biodegradation Test

ld 78-87-5 **Date** 14.12.2004

Year : 1976 GLP : no data

Test substance : other TS: purity > 99 %, [2-14C]-1,2-dichloropropane

Remark: The degradati on grade value is percent of radioactivity.

It relates to the acetone extract of ground sample. The clay ground contained 7 % organic compounds and 30 % humidity. No information was given about controls concerning contaminated

or sterilized ground. The amounts of evaporated 1,2-dichloropropane in vessels were not analyzed. The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : closed system, without ventilation

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (64)

Type : anaerobic Inoculum : other: sandy soil

Concentration : 71 mg/l related to Test substance

related to

Contact time

Source

Degradation : = 20 (±) % after 84 day(s)

Result :

Kinetic of testsubst. : 560 day(s) = 27 %

% % %

Deg. product

Method : other: Biodegradation Test

Year : 1976 GLP : no data

Test substance : other TS: purity > 99 %, [2-14C]-1,2-dichloropropane

Remark: The degradation grade value is percent of radioactivity.

It relates to the acetone extract of the ground sample. The clay ground contained 2 % organic compounds and 15 % humidity. No information was given about controls concerning contaminated or sterilized ground. The amounts of evaporated 1,2-dichloropropane in closed vessels were not analyzed.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : closed system, without ventilation

Reliability : (4) not assignable

Not assignable; Insufficient detail in the I UCLID entry to determine

reliability.

26.10.2004 (64)

Type :

Inoculum : other: sludge

Concentration: 100 mg/l related to Test substance

related to

Contact time

Degradation : = 0 (±) % after 14 day(s)

Result

Deg. product

Method : other: Biodegradation Test

Year : 1974
GLP : no data
Test substance : no data

Remark : 1,2-dichlorpropane is not easily biodegradable.

ld 78-87-5 **Date** 14.12.2004

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (136)

3.6 BOD5, COD OR BOD5/COD RATIO

Remark: Chemical oxygen consumption (CSB) analysis, following the

uniform procedures to test water and waste water, determined that 1,2-dichloropropane can only be oxidized in small quantities by chrome (IV), catalyzed with silver ions.

During the oxidation of dichromate, 12 % of the theoretical CSB value was found without silver ions and 24.5 % with silver ions. 1,2-dichloropropane does not oxidize in the presence of manganese (VII). Oxidation was 0 % of the theoretical value in the presence of permanganate.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (137)

3.7 BIOACCUMULATION

Elimination : Method : Year : GLP :

Test substance : as prescribed by 1.1 - 1.4

Remark : Log BCF

Fish, measured = < 1.0

Calculated = 1.29

Calculated = 1.26

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Data from handbook or collection of data.

Flag : Critical study for SIDS endpoint

25.10.2004 (138) (33)

Species : other: carp (fish) **Exposure period** : 42 day(s) at 25 °C

Concentration

BCF : .5 - 7

Elimination

Method : OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of

Bioconcentration in Fish"

Year : 1981

GLP

Test substance :

Remark : According to the bioconcentration factor (BCF), no or little

bioaccumulation is expected.

Id 78-87-5 **Date** 14.12.2004

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

: pH-value: 7; oxygen content: ca. 7 ppm, flow-through system, direct intake through gills and epithelium. **Test condition**

Test concentration 0.4 and 0.04 mg/L of PDC in water.

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (136)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : flow through

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 139

 Method
 :

Year : 1982 GLP : no data

Test substance: as prescribed by 1.1 - 1.4

Remark : Only brief details are available for this study, which was

conducted as a preliminary to an Early Life Stage test.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Valid with restrictions.

Flag : Critical study for SIDS endpoint

25.10.2004 (139)

Type :

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 140

Limit test

Analytical monitoring : yes

Method: other: US EPA (1975) The Committee on Methods for Toxicity Tests with

Aquatic Organisms: Methods for acute toxicity tests with fish,

macroinvertebrates and amphibians. Ecological Research Series (EPA-

660/3-75-009)

Year : 1983 GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : Test organisms and housing

Laboratory-reared Fathead minnows were used in these studies. The fish were 30 - 35 days old at the time of the

test.

Test conditions

Testing was carried out at 25 degrees C in all-glass aquaria with a working volume 41 l. Water from Lake Superior was used as the exposure medium. Fifty fish were randomly assigned to 12 exposure tanks, comprising five test concentrations plus a control, in duplicate. A 'saturator system' was used to prepare a stock solution of PDC, and the lower exposure concentrations prepared at a dilution spacing of 0.6 (however the actual exposure concentrations used are not stated in the paper). Fish were not fed during the period of the test. Water flow through the tanks was greater than 10 tank volumes per day. Dissolved oxygen, hardness and alkalinity were determined at least once daily on a control, intermediate and high exposure tank. Fluorescent lighting and a 16 hr photoperiod was used (48 lumens at the water

surface).

Analysis

GC with 63Ni electron capture detection was used to quantify

the concentration of PDC in the test solutions.

Determination of LC50

The LC50 concentration was determined using the Trimmer Spearman-Karber method for estimating median lethal concentrations (Hamilton, MA et al. (1977) Environ Sci

Technol, 11, 714; ibid (1978) 12, 417).

Statistics

No further statistical methods were applied to these data. The pH of the test solutions was 6.7 - 7.6, dissolved oxygen

7.6 - 9.2, hardness 45.0 - 45.5 mg/l CaCO3, alkalinity 35.6

- 43.3 mg/l CaCO3).

Recovery of PDC from the exposure solutions was 99 +/- 4%.

General signs of toxicity included lethargy and anaesthesia.

LC50 values (with 95% CI) were as follows:

24 hr = 194 mg/l (184 - 205) 48 hr = 154 mg/l (144 - 166) 72 hr = 141 mg/l (132 - 151) 96 hr = 140 mg/l (131 - 150)

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : The LC50 of PDC in Fathead minnow (Pimephales promelas)

under flow through conditions was 140 mg/l (CI = 131 - 150).

Reliability : (2) valid with restrictions

Test procedure in accordance with national standard methods

and described in sufficient detail.

Flag : Critical study for SIDS endpoint

25.10.2004 (140)

Type : flow through

Species : Limanda limanda (Fish, marine)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 61

 Limit test
 :

Analytical monitoring : no

Result

Method : other: Acute Toxicity Test

Year : 1951 GLP : no data Test substance : no data

Remark: The test was made with non-standardized sea water with

nominal concentration of 1 - 10 mg/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : open vessels, no feeding, temperature: 12 - 18 degrees C,

oxygen content: 5 mg/l

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (141)

Type : flow through

Species : Pimephales promelas (Fish, fresh water)

 Exposure period
 : 24 hour(s)

 Unit
 : mg/l

 LC50
 : = 194

Limit test

Analytical monitoring: no data

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data Test substance : no data

Remark: The 95% confidence level was 184 - 205 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: no feeding, temperature: 23 - 27 degrees C, pH-value: 6.7 -

7.6, hardness: 45.1 mg CaCO3/l, photoperiod: 16 hours light,

8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (140)

Type : flow through

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 LC50
 : = 154

 Limit test
 :

Analytical monitoring : no data

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data Test substance : no data

Remark: The 95% confidence level was 144 - 166 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : no feeding, temperature: 23 - 27 degrees C, pH-value: 6.7 -

7.6, hardness: 45.1 mg CaCO3/l, photoperiod: 16 hours light,

8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (140)

Type : flow through

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 72 hour(s)

 Unit
 : mg/l

 LC50
 : = 141

 Limit test
 :

Analytical monitoring : no data

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data Test substance : no data

Remark: The 95% confidence level was 132 - 151 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: no feeding, temperature: 23 - 27 degrees C, pH-value: 6.7 -

7.6, hardness: 45.1 mg CaCO3/l, photoperiod: 16 hours light,

8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (140)

Type : flow through

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 140

Limit test

Analytical monitoring: no data

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data Test substance : no data

Remark: The 95% confidence value was 131 - 150 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : no feeding, temperature: 23 - 27 degrees C, pH-value: 6.7 -

7.6, hardness: 45.1 mg CaCO3/l, photoperiod: 16 hours light,

8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (140)

Type : semistatic

Species : Poecilia reticulata (Fish, fresh water)

 Exposure period
 : 7 day(s)

 Unit
 : mg/l

 LC50
 : =116

Limit test

Analytical monitoring : no data

Method : other: Prolonged Toxicity Test

Year : 1981 GLP : no data Test substance : no data

Remark : Toxicity was tested on animals 2 - 3 months old.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: The test solution was renewed daily, temperature: 21 - 23

degrees C, oxygen content: 5 mg/l, hardness: 25 mg

CaCO3/I

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (142)

Type : static

Species : Lepomis macrochirus (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 320

Limit test

Analytical monitoring: no

Method : other: Acute Toxicity Test

Year : 1975 GLP : no data Test substance : no data

Remark: The LC50-value was tested based on the nominal

concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: open vessels, no information on feeding, ventilation started

after 24 hours, temperature: 23 degrees C, pH-value: 7.6 -

7.9, hardness: 55 mg CaCO3/I

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (143)

Type : static

Species: Lepomis macrochirus (Fish, fresh water)

 Exposure period
 : 24 hour(s)

 Unit
 : mg/l

 LC50
 : = 360

Limit test

Analytical monitoring : no

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data

Test substance : other TS: purity >= 80 %

Remark: The LC50-value was tested based on the nominal

concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : open vessels, feeding, temperature: 21 - 23 degrees C,

pH-value: 6.5 - 7.9, hardness: 32 - 48 mg CaCO3/l

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (144)

Type : static

Species: Lepomis macrochirus (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 280

 Limit test
 :

Analytical monitoring : no

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data

Test substance : other TS: purity >= 80 %

Remark: The LC50-value was tested based on the nominal

concentration. The 95% confidence level was 220 - 340 \mbox{mg}

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : open vessels, feeding,temperature: 21 - 33 degrees C,

pH-value: 6.5 - 7.9, hardness: 32 - 48 mg CaCO3/l

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (144)

Type : static

Species: Menidia beryllina (Fish, estuary, marine)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 240

Limit test

Analytical monitoring : no

Method : other: Acute Toxicity Test

Year : 1975
GLP : no data
Test substance : no data

Remark : The LC50-value was tested based on the nominal

concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : open vessels, no information on feeding, continuous ventilation, addition of synthetic sea salt mixture

(specific density of the salt solution 1.018), temperature: 20 degrees C, pH-value: 7.6 - 7.9, hardness: 55 mg CaCO3/l

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (143)

Type : static

Species: Pimephales promelas (Fish, fresh water)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 127

Limit test

Analytical monitoring : no data

Method : other: Acute Toxicity Test

Year : 1985 GLP : no data

Test substance : other TS: purity = 99 %

Remark: The 95% confidence level was 119 - 135 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : no information on vessels and feeding, temperature: 25

degrees C, pH-value: 7.5, hardness: 45 mg CaCO3/I

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (145)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : flow through

Species : Daphnia magna (Crustacea)

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 NOEC
 : = 8.3

 EC50
 : = 55.9

 Analytical monitoring
 : yes

Method: other: EPA OTS 797.1330

Year : 1988 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : The acute LC50 of PDC in Daphnia magna was determined as

part of an invertebrate chronic toxicity study.

Test organism and conditions

Daphnia magna brood stocks were acclimated under static

conditions (period not stated) and fed Selenastrum capricorneutum daily throughout the test. Culture medium was carbon-filtered dechlorinated tapwater (hardness 160-180 mg/l CaCO3; pH 8.1-8.3; conductivity 480-624 umho/cm; 8.5-9.4 mg/l oxygen). All glassware was solvent/acid washed prior to use. The test method was based upon EPA OTS 797.1330.

Ten daphnids per treatment level were housed inside a glass exposure chamber, which was placed in a 600 ml glass beakers containing 500 ml of medium. The beakers were loosely covered to reduce volatilisation of PDC from the test solution. The test was conducted at 20 +/- 2 degrees C with a 16 hr light / 8 hr dark cycle but no aeration. Dissolved oxygen, conductivity, pH and temperature in each vessel were recorded at 24 hr intervals during the test.

The calculated nominal concentration of PDC in the test vessels was 0, 7.5, 12.0, 21.0, 36.0 and 60.0 mg/l. The medium inside the test vessels was replaced with fresh medium on average 42 times per day. Samples of test medium were removed from the replicate vessels on days 0, 7, 14 and 21 and analysed using GC (limit of detection 0.02 mg/l).

The number of live daphnids and occurrence of sub-lethal effects (immobilisation, abnormal behaviour, abnormal appearance) were recorded daily.

Statistical analysis

The data were analysed using ANOVA and Dunnett's test, and Probit, moving average and binomial techniques used to calculated the 24 hr and 48 hr LC50.

: Mean, measured concentrations of PDC in the test vessels were 0, 8.3, 15.8, 21.5, 39.5 and 72.9 mg/l.

Physico-chemical parameters recorded daily throughout the 21 days of this flow-through study were as follows:

Oxygen: 8.5-9.4 mg/l

pH: 8.1-8.3

Conductivity: 480-624 umho/cm Temperature: 20.0-21.5 degrees C

Daphnids exposed to 72.9 mg/l DCP were unable to maintain their position in the water column immediately after being placed in the test vessels, while those exposed to 39.5 mg/l were immobilised from day 2. Sub-lethal effects (smaller size, lighter colour) were noted in daphnids exposed to 21.5 mg/l.

There was no mortality at 24 hr or 48 hr in vessels containing 8.3 - 39.5 mg/l PDC. 10-20% mortality was recorded at 24 hr, and 90 - 100% at 48 hr, after exposure to 72.9 mg/l.

The calculated 24 hr and 48 hr LC50 values for lethality in Daphnia magna under flow-through conditions were >72.9 mg/l and 55.9 mg/l, respectively.

: The 1,2-Dichloropropane ICCA/HPV Consortium

: Under the flow-through conditions used in this test, the 48 hr LC50 of PDC in Daphnia magna was 55.9 mg/l.

: (2) valid with restrictions GLP guideline study.

Result

Source Conclusion

Reliability : (2) valid with re

Flag : Critical study for SIDS endpoint

25.10.2004 (146)

Type

Species : Crangon crangon (Crustacea)

Exposure period : 48 hour(s)
Unit : mg/l
LC50 : > 100
Analytical monitoring : no

Method : other: Acute Toxicity Test

Year : 1968 GLP : no data Test substance : no data

Remark: The nominal concentration was tested and the highest level

was 100 mg 1,2-dichloropropane/l.

The LC50-value was tested on adultanimals.

The 1,2-Dichloropropane ICCA/HPV Consortium

static test in sea water, closed vessels, temperature: 15

degrees C, constant ventilation, photoperiod: 24 hours

darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (147)

Туре

Source

Test condition

Species : Daphnia magna (Crustacea)

 Exposure period
 : 24 hour(s)

 Unit
 : mg/l

 LC50
 : = 72.9

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test for Daphnia

Year : 1988 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark : Test conditions: flow-through system, light-covered vessels

with filtrated, dechlorinated tap water.
The stated LC50-value applies to the effective

concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: Temperature: 21 degrees C, pH-value: 8.0 - 8.3, photoperiod:

16 hours light, 8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (146)

Type :

Species : Daphnia magna (Crustacea)

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 LC50
 : = 45

 Analytical monitoring
 : no

Method : other: Acute Toxicity Test for Daphnia

Year : 1984
GLP : no data
Test substance : no data

Remark: The LC50-value was tested based on the nominal

concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : static test, no feeding, temperature: 22 degrees C

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (148)

Type

Species : Daphnia magna (Crustacea)

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 LC50
 : = 55.9

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test for Daphnia

Year : 1988 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark : Test conditions: flow-through system, light-covered vessels

with filtrated, dechlorinated tap water.

The stated LC50-value applies to the effective

concentration.

The 95 % confidence level was 39.5 - 72.9 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: Temperature: 21 degrees C, pH-value: 8.0 - 8.3, photoperiod:

16 hours light, 8 hours darkness

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (146)

Туре

Species : Daphnia magna (Crustacea)

 Exposure period
 : 24 hour(s)

 Unit
 : mg/l

 NOEC
 : < 22</td>

 LC50
 : = 99

 Analytical monitoring
 : no

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data

Test substance : other TS: purity > 80 %

Remark: The stated LC50-value applies to the nominal concentration.

The 95% confidence level was 58 - 600 mg

1,2-dichloropropane/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : static test, temperature: 22 degrees C, pH-value: 7.4-9.4,

hardness: 173 mg CaCO3/I, closed system, no indication on

feeding

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (149)

Туре

Species : Daphnia magna (Crustacea)

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 NOEC
 : < 22</td>

LC50 : = 52 Analytical monitoring : no

Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and

Amphibians, US EPA

Year : 1975 GLP : no data

Test substance : other TS: purity > 80 %

Remark: The stated LC50-value applies to the nominal concentration.

The 95 % confidence level was 42 - 68 mg

1,2-dichloropropane.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Static test, temperature: 22 degrees C, pH-value: 7.4-9.4,

hardness: 173 mg CaCO3/I, closed system, no information on

feeding.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (149)

Туре

Species : Mysidopsis bahia (Crustacea)

 Exposure period
 : 24 hour(s)

 Unit
 : mg/l

 LC50
 : > 26.65

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test

Year : 1967 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark: The tests were made in animals < 24 hours in a flow-through

system. The average, actual concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentrations. The authors attribute this to the evaporation. The stated LC50-value was calculated in

appliance to the actual concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: The animals were exposed to 5 different concentrations of

1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered seawater (salinity: 20 - 21 o/oo), with feeding, temperature: 25

degrees C, photoperiod: 14 hours light, 10 hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (150)

Type

Species : Mysidopsis bahia (Crustacea)

 Exposure period
 : 72 hour(s)

 Unit
 : mg/l

 LC50
 : = 24.79

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test

Year : 1967 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark: The tests were made in animals < 24 hours in a flow-through

system. The average actual concentrations per dilution were

between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentration. The authors attribute this to the evaporation. The stated LC50-value, referred to the actual concentration with a 95 % confidence level, was calculated

as

4.92 - infinity mg/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50

1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered sea-water (salinity: 20 - 21 o/oo), with feeding,

temperature: 25 degrees C, photoperiod: 14 hours light, 10

hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (150)

Туре

Species : Mysidopsis bahia (Crustacea)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : = 24.79

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test

Year : 1967 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark : The tests were made in animals < 24 hours in a flow-through

system. The average, actual concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentrations. The authors attribute this to the evaporation. The stated LC50-value was calculated in

appliance to the actual concentration.

The mortality after 96 hours averaged between 5 % with 4.92 mg/l (actual) concentration and 55 % with the highest tested (actual) concentration of 26.55 mg/l. The LC50-value was applied to the actual concentration of 4.92 - infinite mg/l

with a 95 % confidence level.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : The animals were exposed to 5 different concentrations of

1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered

sea-water (salinity: 20 - 21 o/oo), with feeding,

temperature: 25 degrees C, photoperiod: 14 hours light, 10

hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (150)

Type :

Species: Mysidopsis bahia (Crustacea)

 Exposure period
 : 96 hour(s)

 Unit
 : mg/l

 LC50
 : > 26.65

 Analytical monitoring
 : yes

Method : other: Acute Toxicity Test

Year : 1967

GLP : no data

Test substance : other TS: purity = 99.9 %

Remark: The tests were made in animals 3 - 4 days old in a

flow-through system. The average, actual

concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/I nominal) and 53 % (with 50 mg 1,2-dichloropropane/I nominal) of the nominal concentration. The authors attribute this to the evaporation. The stated LC50-value was calculated in appliance to the actual

concentration.

The mortality after 96 hours averaged 0 % (with 4.92 mg 1,2-dichloropropane/l) and 30 % (with 10.88 and 26.55 mg 1,2-dichloropropane/l). These results estimated the

LC50-value.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: The animals were exposed to 5 different concentrations of

1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered sea-water (salinity: 20-21 o/oo), with feeding, temperature: 25

degrees C, photoperiod: 14 hours light, 10 hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (150)

Type

Species : other aquatic crustacea: Eliminius modestus

 Exposure period
 : 48 hour(s)

 Unit
 : mg/l

 LC50
 : = 53

 Analytical monitoring
 : no data

Method : other: Acute Toxicity Test

Year : 1975
GLP : no data
Test substance : no data

Remark: The test medium did not follow standardized conditions,

therefore, only a limited comparison is possible. The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Static test, closed vessels

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (141)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Skeletonema costatum (Algae)

Endpoint : biomass Exposure period : 120 hour(s) Unit : ma/l

NOEC : = 7.4 - 18 measured/nominal

Limit test

Source

Analytical monitoring : yes

Method : EPA OTS 797.1050

Year : 1988 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

ld 78-87-5 Date 14.12.2004

Method

: Test organism and conditions

Skeletonema costatum in logarithmic growth phase and grown on synthetic marine algal assay nutrient medium was used as the inoculum for the test. All glassware was thoroughly cleaned with non-phosphate detergent, then rinsed with hydrochloric acid, deionised water and medium prior to use. Assavs (volume 25 ml) were conducted in 125 ml Erlenmeyer flasks fitted with Teflon-lined screw-capped lids. One set of replicate flasks was prepared for each study day, and discarded after sampling.

Range finding test

A range finding test was conducted to determine concentrations to be used in the definitive study. Assays were conducted in duplicate, with nominal concentrations of 1, 10, 100 and 1000 mg/l. Exposure was for 5 days. Analysis of PDC content was performed on study days 0, 3 and 5.

Definitive test

Five test concentrations (10, 18, 32, 56 and 100 mg/l) and a control were prepared in triplicate. Analysis of the PDC content of the flasks (GC -FID) was carried out on study days 0, 2, 3, 4 and 5. Algal biomass (Coulter counter, 3 counts per replicate) was determined on days 2, 3, 4 and 5 of the exposure phase, and again during a recovery phase (see below). A parallel set of control flasks with foam stoppers was also prepared to monitor algal growth under conditions open to the atmosphere.

Microscopic counts of individual cells (improved Neubauer hemacytometer) were also made on one flask each of the highest test concentration, an intermediate test concentration and a control on day 5 of the study.

The cultures were incubated at 20 (+/-2) degrees C with illumination of 4306 (+/-646) lux with a photoperiod of 14 hr light:10 hr dark. Flasks were shaken manually on each sampling day.

Determination of algistatic and algicidal effects Aliquots from the 56 mg/ml and 100 mg/ml vessels (where culture counts were similar to or lower than the initial inoculum level) were either subcultured into fresh medium and cell growth determined on days 2, 6 and 9 (recovery experiment), or stained with Evans Blue stain and examined microscopically (living cells exclude stain).

AUC calculation to estimate PDC content of test medium Due to the highly variable results obtained from the analytical determinations, the measured water dissipation rates for PDC in algal medium were determined by Woodburn and used to calculate the overall residual amounts of test substance present in the flasks. This was expressed as the time weighted average (TWA) concentration, and was based upon the area under the concentration curve. It follows methods developed in Annex 6 of the updated OECD Guideline 202, part II (Daphnid reproduction test, revised January 1996). The integrated area is considered by OECD to be the best expression of the dose to which aquatic organisms are exposed over the selected time period. Further information is given in Attachment 4.3AUC.

4. Ecotoxicity

ld 78-87-5 **Date** 14.12.2004

Statistical analysis

Analysis of variance and two multiple range tests (Tukey's test, Scheffe's test) were applied to the cell count data.

Remark

Although closed vessels were used, significant loss of PDC from the test vessels was evident. While a general trend of decreasing algal growth with increasing nominal exposure concentration was apparent, the analysed concentrations for each nominal value were sufficiently variable to preclude determination of an EC50 value from the data. The data were, however, adequate for derivation of a NOEC value. The reliability of this determination has been enhanced through additional 'area under the curve' calculations performed subsequently by scientists from the laboratory performing the study.

Result

: Analytical results

Mean analysed concentrations on day 1 were in a range 57-75% of nominal. From day 2 onwards, however, there was little consistency either between results obtained within a set of replicate flasks or between the analysed and nominal concentrations. It was concluded that significant losses had occurred despite use of screw-capped vessels.

Calculated TWA concentrations

The calculated TWA concentrations for PDC on exposure days 3, 4 and 5 are shown in Attachment 4.3a. The application of first-order kinetics to the dissipation of PDC in algal media is presented in Attachment 4.3b.

Cell counts

Mean values for the three replicate flasks were highly variable, reflecting the analytical results. This information is summarised in Attachment 4.3c. No clear concentration-response relationship is evident, as would be expected given the analytical results, although there was a trend of reduced algal growth in the two highest nominal test concentrations.

Comparison of mean cell counts from the screw-capped- and foam stoppered controls revealed a 65-73% reduction in growth in the capped vessels.

Microscopic counts were lower than counts obtained using the Coulter counter, however this did not appear to have any significant impact on the overall interpretation of the data.

Little growth occurred in algal populations from the two highest test concentrations during the recovery period. Growth in the control samples was also poor, suggesting that insufficient cells had been used to inoculate the recovery vessels. No conclusion could therefore be reached concerning possible algistatic and algicidal effects of PDC.

Microscopic examination of Evans blue stained cells from the 56 mg/l and 100 mg/l vessels was inconclusive since it was difficult to discriminate between stained and unstained cells. Approx. 8% of cells from the 56 mg/l culture, and 20% of cells from the 100 mg/l culture, appeared dead.

Determination of IC50 value

No scientifically valid estimate of the IC50 for PDC was possible given the highly variable results obtained for

algal growth and analysed concentration.

No Observed Effect Concentration

ANOVA and multiple range tests indicated that there were no significant differences between mean cell counts in the 10 mg/l and 18 mg/l nominal concentrations and the controls on any of the exposure days. In contrast, mean cell counts obtained from the other concentrations did differ

significantly from controls. The authors conclude that the 5 day NOEC for PDC in Skeletonema costatum is 18 mg/l

(nominal).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 4.3 AUC.doc

Attachment 4.3a.doc Attachment 4.3b.doc Attachment 4.3c.doc

Conclusion: Under the conditions of the test, the 5-day NOEC for PDC in

Skeletonema costatum was 18 mg/l based on nominal values,

and 7.4 mg/l using analysed concentrations and a TWA technique to integrate the dose to which the algae were

exposed.

Reliability : (2) valid with restrictions

Guideline study using accepted calculation method,

acceptable with restrictions.
Critical study for SIDS endpoint

25.10.2004 (151) (152) (153)

Species : Skeletonema costatum (Algae)
Endpoint : other: biomass and growth rate

Exposure period : 72 hour(s) **Unit** : mg/l

EC50 : = 14.7 - 16.3 calculated

Method : other: calculation

Year GLP

Flag

Test substance: as prescribed by 1.1 - 1.4

Method : Algal biomass- and growth measurements from the algal

toxicity study in Skeletonema costatum study reported by Hughes (1998) were used by Woodburn (2002a,b) to derive a 120 hr NOEC and a 72 hr EC50 value, based upon calculated time-weighted average concentrations of PDC in the test medium. [For details of the TWA calculation, see attachment

4.3 AUC and Attachment 4.3a).

Result : Attachment 4.3d tabulates the percentage biomass inhibition-

and inhibition of growth rate reported by Hughes (1988) against the TWA concentration of PDC in the test system

calculated by Woodburn (2002a).

The figures in Attachment 4.3d present graphical plots of

this information.

Based on this analysis, the 72 hr EC50 (biomass) for PDC in Skeletonema costatum is 16.3 mg/l, while the 72 hr EC50 $\,$

(growth) is 14.7 mg/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 4.3 AUC.doc

Attachment 4.3a.doc Attachment 4.3d.doc

Conclusion: Based on this re-analysis, the 72 hr EC50 for

1,2-dichloropropane in Skeletonema costatum is 14.7 -16.3

mg/l.

Reliability : (2) valid with restrictions

Reanalysis of data using accepted calculation methods.

Flag : Critical study for SIDS endpoint

25.10.2004 (154)

Species: Skeletonema costatum (Algae)Endpoint: other: biomass and growth rate

Exposure period : 72 hour(s)
Unit : mg/l

NOEC : = 8.9 calculated

EC50 : = 15.1 - 15.8 calculated

Method : other: calculation

Year GLP

Test substance : as prescribed by 1.1 - 1.4

Method : The cell density measurements from Hughes (1988) were used

to calculate the biomass integral (day 3) and growth rate

(days 0-3) for each test flask.

These results were used to determine the mean biomass integral and mean growth rate for each test concentration. The inhibition (%) of the biomass integral and the inhibition (%) of the growth rate were then calculated for each test concentration.

Linear interpolation, with concentration on a logarithmic scale (base = 10), was used to determine the EC50 over 0-72h

for biomass integral and growth rate inhibition.

Details of the calculations used are given in Attachment

4.3e.

Result : Although the variation in the measured concentrations

between replicates was relatively high a good

concentration-response relationship was obtained after 3

days of exposure (see Attachment 4.3e).

Using linear interpolation, with mean measured

concentrations on a logarithmic scale (base = 10), the EC50 over 0 - 72h for biomass integral and growth rate were 15.8

and 15.1 mg/l, respectively.

The No Observed Effect Concentration (NOEC), based on biomass integral at test termination, was determined with Williams' Test (Williams, 1972). Based on mean measured

concentrations this revealed a NOEC of 8.9 mg/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 4.3 e.doc

Conclusion: Based on this re-analysis, the 72 hr EC50 for

1,2-dichloropropane in Skeletonema costatum is 15.1 -15.8

mg/l, with a 72 hr NOEC of 8.9 mg/l.

Reliability : (2) valid with restrictions

Reanalysis of data using accepted calculation methods.

Flag : Critical study for SIDS endpoint

25.10.2004 (151)

Species : Phaeodactylum tricornutum (Algae)

Endpoint : biomass

Exposure period

Unit : mg/l EC50 : = 50 Limit test :

Analytical monitoring: no data

Method : other: Algae, Assimilation Inhibition Test

Year : 1975
GLP : no data
Test substance : no data

Remark: The retardation of the 14C-assimilation was investigated.

The test medium (seawater) did not follow standardized conditions, therefore, only a limited comparison is

possible.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (141)

Species : Selenastrum capricornutum (Algae)

Endpoint : growth rate

Exposure period

Limit test

Analytical monitoring : yes

Method : other: Algae Inhibition Test

Year : 1987 GLP : no dat

Test substance : other TS: purity = 99.9 %

Remark : The cell increase was tested at the end of days 2, 3, 4 and

5.

After 5 days there was no longer correlation between the nominal and the actual concentration due to "variable evaporation" from the closed vessels. They could not establish a correlation between the actual concentration and growth of the cell chains. The NOEC corresponds to the

highest tested concentration.

In relation to the average number of algae (high standard deviation) for days 2, 4 and 5, there was no difference in the growth compared with the nominal concentration of 1000 mg 1,2-dichloropropane/l. On the other hand, day 3 showed a significant difference in the average cell number for 180, 560 and 1000 mg 1,2-dichloropropane/l (nominal).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : The algae was exposed for 5 days to 5 different

1,2-dichloropropane concentrations (nominal: 100, 180, 320,

560 and 1000 mg/l), static test, closed vessels,

temperature: 22 - 26 degrees C, photoperiod: continuous

exposure.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (155)

Species : Skeletonema costatum (Algae)

Endpoint : growth rate

Exposure period

Unit : mg/l **NOEC** : = 18

Limit test :

Analytical monitoring : yes

Method : other: Algae Inhibition Test

Year : 1987

GLP : no data

Test substance : other TS: purity = 99.9 %

Remark: The cell numbers, established after days 2, 3, 4 and 5, were

the parameters. The NOEC based on the nominal concentration was estimated since no correlation between the nominal and

the actual concentration was found.

Endpoints applied to cell growth (EC-values) could not be determined on the basis of the respective measured concentration (in consideration of time and method) as there was only a tendency but no strict correlation between the

actual concentration and the biological effect.
The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : The algae was exposed to 5 different concentrations of

1,2-dichloropropane (nominal: 10, 18, 32, 56 and 100 mg/l) closed vessels, temperature: 18 - 22 degrees C, pH value 7.5

- 7.6, photoperiod: 14 hours light, 10 hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (152)

Species : Skeletonema costatum (Algae)

Endpoint : Exposure period : Unit :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004

Source

Source

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic

Species : activated sludge, domestic

Exposure period : Unit :

Analytical monitoring : no data

Method : other: OECD Guide-line 301 D

Year : 1981 GLP : no data

Test substance : other TS: purity = 65 %

Remark: After 28 days no significant inhibition of oxygen intake of

domestic, activated sludge was established using Na-Benzoate

with 3 mg 1,2-dichloropropane/l.

A mixture with 1,2-dichloropropane as the main component was

tested. Other components of the mixture were:

1,3-dichloropropene25%2,3-dichloropropene10%1,1-dichloropropenetrace3,3-dichloropropenetrace

: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (127)

Type : aquatic

Species: other bacteria: BASF-activated sludge

 Exposure period
 : day(s)

 Unit
 : mg/l

 EC50
 : = 630

 EC80
 : = 1400

 EC20
 : = 290

 Analytical monitoring
 : no data

Method : other: not specified

Year

GLP : no data

Test substance

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (135)

Type : aquatic

Species : other bacteria: BASF-activated sludge

Exposure period: day(s)Unit: mg/lEC20: = 1300Analytical monitoring: no data

Method : other: not specified

Year

GLP : no data

Test substance :

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (156)

Type : field

Species: other bacteria: autochthone microorganisms

Exposure period : 16 hour(s)
Unit : mg/l
MEC : = 1700
Analytical monitoring : no data

Method : other: Bioluminescence

Year : 1986
GLP : no data
Test substance : no data

Remark: The inhibitive effect of 2,3-dichloropropane was tested on

autochthone microorganisms from water samples of pristine aquifer. The ATP concentration in water was determined with

bioluminescence. The MEC value (minimum effect concentration) is the lowest value which results in a

significant inhibition.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Incubation temperature: 10 degrees C, measure temperature:

25 degrees C, integration time: 10 seconds.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (157)

4.5.1 CHRONIC TOXICITY TO FISH

Species: Pimephales promelas (Fish, fresh water)

Endpoint : other: survival, growth

 Exposure period
 : 28 day(s)

 Unit
 : mg/l

 NOEC
 : = 6 - 11

 Analytical monitoring
 : yes

 Method
 :

Year : 1982 GLP : no data

Test substance: as prescribed by 1.1 - 1.4

Method : General

Prior to starting the Early Life Stage (ELS) test, the 96 hr LC50 was determined using 30 day old fish. This was followed by 6-10 day range-finding test using 24 hr old larvae. The objective of both tests was to identify the lowest concentration that caused abnormal behaviour (erratic swimming, lethargy, decreased feeding etc) in the test organisms. This concentration was used as the highest concentration for the ELS study.

Test organisms and housing

All organisms were reared in the laboratory performing the study. Exposure of eggs and larvae took place in glass tanks (nominal volume 500 ml, water depth 4.5 cm) under continuous flow conditions (90% of the test solution replaced every 75 min).

For the main ELS test, 30 eggs (2-8 hr old) were placed in 4 replicate tanks per exposure concentration and observed until hatching (ie 4-5 days post-spawn). Fifteen healthy larvae per tank were then selected at random, placed in each of 4 replicate chambers and sur vival followed for 28 days. Body weight was determined at the end of the test. The fish were fed shrimp nauplii throughout the study.

Test conditions

Filtered, UV-sterilised water was obtained from Lake Superior, and had the following characteristics: hardness 45 mg CaCO3/l; alkalinity 42 mg CaCO3/l; pH 7.4; dissolved oxygen 7 mg/l. Illumination was provided by cool white fluorescent lamps with a 16 hr light period. Water temperature was 25 degrees C. Exposure concentrations of 0, 6, 11, 25, 51 and 110 mg/l (obtained by diluting a stock saturated solution of PDC in water) were used.

Analytical

The concentration of PDC in the tanks was measured twice per week in alternate replicate tanks using GC (limit of detection 0.1 mg/l).

Statistics

Hatchability of embryos, normal larvae at hatch and survival and mean weight and length data were subject to ANOVA with an F test and Dunnett's test.

Remark : Inspection of the results from this study provides the

following NOEC values (LOEC in brackets):

Hatchability: 110 mg/l (>110 mg/l)

Normal larvae at hatch: 25 mg/l (51 mg/l) Survival to day 28: 11 mg/l (25 mg/l) Weight at day 28: 6 mg/l (11 mg/l)

: Measured exposure concentrations were 0, 6, 11, 25, 51 and

110 mg/l.

Embryo hatchability was 96% - 98%, with no treatment-related differences apparent, however the percentage of normal larvae was decreased significantly in the 51 mg/l and 110 mg/l tanks (decreased 33% and 100%, respectively).

Body weight at day 28 was reduced significantly in larvae exposed to 11 mg/l and above, while larval survival was

significantly decreased at 25 mg/l and above.

The authors estimate that the Maximum Acceptable Toxicant

Concentration (MATC, defined as a hypothetical toxic

threshold falling mid-way between the NOEC and LOEC) for PDC

is 59 mg/l.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Under the conditions of this ELS test in Fathead minnows, a

chronic NOEC of 6 mg/l was obtained for growth and a chronic

NOEC of 11 mg/l obtained for survival.

Reliability : (2) valid with restrictions

Test procedure in accordance with generally accepted scientific methods and described in sufficient detail.

Flag : Critical study for SIDS endpoint

25.10.2004 (139)

Species: Pimephales promelas (Fish, fresh water)

Endpoint : other: weight of young fish

 Exposure period
 : 28 day(s)

 Unit
 : mg/l

 MATC
 : = 5 - 12

 Analytical monitoring
 : yes

Result

Method : OECD Guide-line draft "Early Life Stage Test (ELS-Test)"

Year : 1976 GLP : no data Test substance : no data

Remark: The test was made with eggs 2 - 5 days old. An exposition to

25 mg 1,2-dichloropropane/l significantly (p = 0.05) delayed the survival rate of the fish after 28 days. A concentration of 51 mg/l, measured in flow-through, caused a significantly (p = 0.05) higher deformity rate in the hatched larva. The MATC-value gives the hypothetical toxic threshold

concentration, which is located as the geometrical average between the concentration that causes no effect (NOEC). The next level tested caused a significant toxic effect (LOEC).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (139)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)

Endpoint : reproduction rate

Exposure period : 21 day(s)

ld 78-87-5 4. Ecotoxicity Date 14.12.2004

Unit mg/l

NOEC = 8.3 measured/nominal LOEC = 15.8 measured/nominal

Analytical monitoring

Method EPA OTS 797.1330

Year

GLP

Test substance as prescribed by 1.1 - 1.4

Method : Test organism and conditions

> Daphnia magna brood stocks were acclimated under static conditions (period not stated) and fed Selenastrum capricorneutum daily throughout the test. Culture medium was carbon-filtered dechlorinated tapwater (hardness 160-180 mg/l CaCO3). All glassware was solvent/acid washed prior to use. The test method was based upon EPA OTS 797.1330.

Ten daphnids per treatement level were housed inside a glass exposure chamber, which was placed in a 600 ml glass beakers containing 500 ml of medium. The beakers were loosely covered to reduce volatilisation of PDC from the test solution. The test was conducted at 20 +/- 2 degrees C with a 16 hr light / 8 hr dark cycle but no aeration. Dissolved oxygen, conductivity, pH and temperature in each vessel were recorded at 24 hr intervals during the test.

The calculated nominal concentration of PDC in the test vessels was 0, 7.5, 12.0, 21.0, 36.0 and 60.0 mg/l. The medium inside the test vessels was replaced with fresh medium on average 42 times per day. Samples of test medium were removed from the replicate vessels on days 0, 7, 14 and 21 and analysed using GC (limit of detection 0.02 mg/l).

The number of live daphnids and occurrence of sub-lethal effects (immobilisation, abnormal behaviour, abnormal appearance) were recorded daily.

Statistical analysis

The data were analysed using ANOVA and Dunnett's test, and Probit, moving average and binomial techniques used to calculated the 24 hr and 48 hr LC50. The 21-day NOEC and LOEC were calculated by observing which concentration

produced responses.

Mean, measured concentrations of PDC in the test vessels were 0, 8.3, 15.8, 21.5, 39.5 and 72.9 mg/l.

Daphnids exposed to 72.9 mg PDC/I were unable to maintain their position in the water column immediately after being placed in the test vessels, while those exposed to 39.5 mg/l were immobilised from day 2. Sub-lethal effects (smaller size, lighter colour) were noted in daphnids exposed to 21.5 mg/l.

The 21 day NOEC for reproduction was 8.3 mg/l and the LOEC 15.8 mg/l.

The 21 day NOECs and LOECs for sub-lethal effects (immobilisation, size, colour) and death were 15.8 mg/l and the LOEC 21.5 mg/l, respectively.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Under the flow-through conditions used in this test, the 48 hr LC50 of PDC in Daphnia magna was 55.9 mg/l, while the 21

90/90

Result

Conclusion

day NOEC and LOEC for reproduction were 8.3 mg/l and 15.8

mg/l, respectively.
(2) valid with restrictions

Reliability : (2) valid with restrictions GLP quideline study.

: Critical study for SIDS endpoint

25.10.2004 (146)

Species : Mysidopsis bahia (Crustacea)

Endpoint : other: parental mortality, number of young per female, adult growth

 Exposure period
 : 28 day(s)

 Unit
 : mg/l

 NOEC
 : >= 4.09

 Analytical monitoring
 : yes

Flag

Remark

Method : EPA OTS 797.1950

Year : 1989 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method: Test organism and conditions

Mysid cultures (<24 hr old) were maintained in natural sea water (salinity: 20 parts per thousand) at 25 degrees C for

10 days pri or to starting the test.

Exposure of the test organisms took place in glass aquaria (vol approx 6.8 l). Fresh medium, containing PDC, was pumped into each aquarium and provided approx. 11.8 volume additions per day. The mysids were fed brine shrimp nauplii during the test.

The final nominal concentration of PDC in the vessels was 0, 0.6, 1.2, 2.3, 4.6 and 9.3 mg/l (each in duplicate). Water samples were collected from the chambers on study days 0, 7, 14, 21 and 28 and their PDC content analysed using GC-electron capture.

At the start of the test, 40 post-larval mysids per treatment were selected at random and evenly distributed between four

chambers housed within two replicate vessels per treatment. On test day 16, each female within a treatment replicate was paired with a male from the same treatment group, the pairs isolated within their treatment groups until study termination. The number of dead mysids, the time to release of broods, length of adults on day 15 and the number of off-spring produced were recorded. (All off-spring were maintained in the same test concentration as the parents until the end of the test.)

Salinity, temperature and dissolved oxygen were measured regularly during the test.

Statistical analysis

The data were analysed using AN OVA and Dunnett's test after verifying homogenity of the variances using Bartlett's test.

The NOEC for parental and larval mortality, number of

off-spring per female and time to release of first brood, and adult growth was 4.09 mg/l.

Result : Analysed exposure concentrations

Mean analysed concentrations of PDC in the test vessels were 0.41, 0.97, 1.35, 2.48 and 4.09 mg/l, however mechanical problems with the diluter apparatus meant that individual analysed values on days 0 -28 were variable (i.e. in a range

0.36-0.61, 0.51-1.83, 1.24-1.57, 1.89-3.20 and 2.96-4.99 mg/l for the 0.6, 1.2, 2.3, 4.6 and 9.3 mg/l exposure groups, respectively).

Mortality

Parental mortality varied from 22% in cultures exposed to 0.97 or 1.35 mg PDC/l to 28% in cultures exposed to 0.41 or 4.09 mg/l. Mortality in controls was 10%. There was no statistically significant difference between mortality in the control or treated groups. Overall survival of juveniles

treated parents varied from 85% in the 4.09 mg/l group to 91% in the 0.41 mg/l group, with 85% survival in the controls.

Number of off-spring and time to first brood release
The average number of off-spring per female varied from 6.8 in the 4.09 mg/l group to 10.6 in the 2.48 mg/l group, with 11.3 young/female in the controls (not significant). Mean time to first brood release was 15.5 or 16.0 days in the treated mysids versus 16.5 days in the controls. These differences were not statistically significant.

Adult growth

Mean length of adults after 15 days and 28 days exposure, and adult weight at termination, were unaffected by treatment.

Source Conclusion

Reliability

The 1,2-Dichloropropane ICCA/HPV Consortium
 Under the conditions of the test, the 28 day NOEC for mortality, reproduction and growth in the mysid shrimp o ver 28 days was at least 4.09 mg/l, the highest concentration tested.

(158)

: (2) valid with restrictions

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004

Species: Mysidopsis bahia (Crustacea)

 Endpoint
 : mortality

 Exposure period
 : 28 day(s)

 Unit
 : mg/l

 NOEC
 : = 4.09

 Analytical monitoring
 : yes

Method : other: Chronic Toxicity Test

Year : 1988 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark

: The test was made in lightly covered vessels, using through-flow system, with naturally filtered seawater. The chronic toxicity was tested on animals < 24 hours old. The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 0.6, 1.2, 2.3, 4.6 and 9.3 mg/l).

No significant effects were observed on the parameters' parents and F1 mortality, longitudinal growth of the parents and on reproduction for the highest tested actual concentration of 4.09 mg/l (^= NOEC). The actual

concentration varied as the dilution and mixboxes were

modified three times.

In rating the tests one must consider that the average measured concentrations (related to the dilution level) were

between 0.41 - 4.09 mg/l - this means 81 % - 44 % of the

nominal concentration.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature: 23 - 28 degrees C, salinity: 18 - 25 o/oo,

pH-value: 7.3 - 8.3, photoperiod: 14 hours light, 10 hours

darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (159)

Species : Daphnia magna (Crustacea)

Endpoint : reproduction rate
Exposure period : 21 day(s)
Unit : mg/l

Method : other: Toxic Substance Control Act Test Guidelines, Final Rules, US EPA

Year : 1985 GLP : no data

Test substance : other TS: purity = 99.9 %

Remark: The test was made in lightly covered vessels, in

thorugh-flow system, with filtered, de-chlorinated tap water. The animals were exposed to 5 different concentrations (nominal: 60.0, 36.0, 21.0, 12.0 and 7.5 mg/l). To measure sub-lethal effects, immobilization and

abnormal swimming behavior was used.

Other parameters were mortality, reproduction and unchanged look. The average actual concentrations were between 102 -

132 % of the nominal concentration.

The MATC value gives the toxic threshold concentration, which is the geometrical average between the concentration which causes no toxic effect (NOEC) and the next tested level that causes significant toxic effects (LOEC).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: Temperature: 18 - 22 degrees C, hardness: 160 - 180 mg

CaC03/I, photoperiod: 16 hours light, 8 hours darkness.

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (146)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type : artificial soil

Species : Eisenia fetida (Worm (Annelida), soil dwelling)

 Endpoint
 : mortality

 Exposure period
 : 14 day(s)

 Unit
 : mg/kg soil dw

 LC50
 : = 4240

Method : OECD Guide-line 207 "Earthworm, Acute Toxcity Test"

Year : 1981 **GLP** : no data

Test substance : other TS: purity = 98 %

Remark: A mixture of peat, clay, fine sand and calcium carbonate

served as test medium. Ten adult animals weighing between 300 - 500 mg were exposed to 1,2-dichloropropane. The 95 % confidence level was 3830 - 4680 mg 1,2-dichloropropane/kg

of dry ground mass.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature: 20 degrees C, pH-value: 5.5 - 6.5, ground

humidity: 35%

Reliability : (2) valid with restrictions

Guideline study

25.10.2004 (160)

Type : artificial soil

Species : Eisenia fetida (Worm (Annelida), soil dwelling)

Endpoint : other: growth
Exposure period : 56 day(s)
Unit : mg/kg soil dw
LC0 : = 92300

Method : other: Earthworm, Toxicity Test

Year : 1990 GLP : no data Test substance : no data

Remark: Test medium were organic dung, sand and deionized water.

The animals which were exposed to 1,2-dichloropropane were < 7 days old and weighed < 10 mg. Concentrations up to 80.8

g

1,2-dichloropropane/kg did not cause significant changes in the average weight of the animals or in the reproduction rate (parameter was number of cocoons/worms).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : uncovered Petri dish, temperature: 25 degrees C, ground

humidity: 70 - 80 %

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (161)

Type : filter paper

Species : Eisenia fetida (Worm (Annelida), soil dwelling)

Endpoint : mortality
Exposure period : 48 hour(s)
Unit : mg/cm² filter paper

LC50 : = .064

Method : OECD Guide-line 207 "Earthworm, Acute Toxcity Test"

Year : 1981 GLP : no data

Test substance : other TS: purity = 98 %

Remark: Weight of animals exposed to 1,2-dichloropropane was between

300-500 mg. The 95% confidence level was 0.059-0.07 mg

1,2-dichloropropane/cm2.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition : Temperature: 20 degrees

Incubation at dark

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (160)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo : In vivo Type : Distribution

Species : rat

Number of animals

Males : 4 Females : 4

Doses

 Males
 : 5, 50 or 100 ppm

 Females
 : 5, 50 or 100 ppm

Vehicle : other: air

Route of administration : inhalation Exposure time : 6 hour(s)

:

Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :

Half-lives

1st: 2nd: 3rd:

Toxic behaviour
Deg. product

Method : other: EPA test rule study

Year : 1989 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male (121-136 g) and female (106-124) F344 rats (7 wk old, n=4/sex) were exposed (head only) for 6 hr to 5, 50 or 100 ppm 14C-labeled PDC under dynamic flow conditions. The

concentration of radioactivity in plasma and the

concentration of PDC in whole blood were determined during

and after exposure (cannulated jugular vein).

Chambers, atmosphere and analysis

The chamber was constructed of Teflon-lined plastic, and allowed the simultaneous exposure of 8 rats (4 male, 4 female; housed on two tiers) during exposure. It was designed to permit collection of blood samples during exposure. Vapors were generated by pumping the contents of SARAN bags filled with measured volumes of 14C-PDC and dry compressed air into the chambers. The concentration of PDC at one point in the upper and the lower tier was determined by GC/FID, with LSC to quantify the concentration of

radio-label.

Analysis of blood

Aliquots of blood were pooled (by sex and time interval) and analysed by GC/MS for quantity of PDC present.

Other details

All other methods etc were as decribed in the preceeding

record.

Result : The measured concentration of PDC in the chambers was

4.6/4.7 ppm, 52.4/56.8 ppm and 141.8/125.2 ppm for males/females, respectively, in the low, mid and high exposure groups, respectively. Mean end exposure body burdens were 0.4/0.3, 2.8/2.8 and 6.3/7.1 mg equivalents of

PDC for males/females in the low, mid and high exposure groups, respectively.

The distribution of recovered radioactivity is summarized in Attachment 5.0b. In summary, urine (54-66% of recovered dose) and expired air (15-23% as carbon dioxide) were the principle routes of excretion with smaller amounts present in tissues and carcass (6-10%) and faeces (6-10%). Less than 4% of the recovered radioactivity was present in cage washings. Exhaled volatiles accounted for 2-3% of the dose in animals exposed to 5 ppm and 50 ppm, and 6-7% in the 100 ppm group (high dose group significantly different from mid and low dose groups). The pattern of excretion did not differ between males and females.

Analysis of tissues

Radioactivity was distributed among all the tissues examined and generally represented less than 0.18% of the recovered dose/g wet weight. The liver and kidneys contained the highest amount of radioactivity, accounting for 0.1-0.3% and 0.1-0.2% of the dose/g wet weight, respectively. There were no obvious differences in tissue distribution between the sexes or in distribution or concentration for the different exposure concentrations.

Timecourse for elimination

Urinary elimination of radiolabel was greatest over the first 24 hr post-dosing (47-62% of dose) relative to the following 24 hr (2-9%). Comparative figures for exhaled carbon dioxide were 13-20% and <3%, and 5-8% and 0.7-3.0% for faeces (at 0-24 and 24-48 hr, respectively). The majority of exhaled volatiles were also eliminated during the

24 hr following exposure, with <0.03% detected during the 24-48 hr time period.

Blood concentrations in both sexes were generally at a maximum 4 hr into the exposure (exception: 5 ppm females which peaked at 1 hr). In both sexes the peak blood PDC level was not proportional to dose indicating a dose-dependent non-linearlity in clearance. The concentration in blood was below the limit of detection (0.03 ug/g) 2 hr after exposure ended. Modelling (one-compartment open model with linear fit) indicated a post-exposure blood clearance half life for PDC of 30 min in males and 24 min in females.

In plasma, the highest concentration of 14C in both sexes was found at 4 hr in the exposure, and ranged from 2, 12-15 and 27-29 ug eq/g plasma present in the 5, 50 and 100 ppm groups respectively. Corresponding AUCs were 21-23, 130-134 and 288-320 ug g^1, respectively. Comparison of the 5 ppm peak plasma 14C level and AUC with the mid- and high dose groups indicated that plasma 14C was less than proportional to dose.

Metabolites

Approx. 60-90% of the radioactivity present in the exhaled volatile fraction was unchanged PDC. HPLC analysis of urine (pooled from the 3 inhalation experiments) revealed the presence of three n-acetylcysteine conjugates of PDC

(N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine and

N-acetyl-S-(2-carboxyethyl)-L-cysteine) but no detectable parent compound. Attempts to identify four other HPLC peaks

were unsuccessful.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 5.0b.doc

Conclusion: Urine and exhaled carbon dioxide were the principle routes

for elimination of PDC in male and female rats after 6 hr inhalation exposure to 5, 50 or 100 ppm. The majority of

radioactivity was excreted within 24 hr, with little

unchanged PDC present.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (162)

In Vitro/in vivo : In vivo
Type : Distribution

Species : rat

Number of animals

Males : 4 Females : 4

Doses

Males : 1 or 100 mg/kg
Females : 1 or 100 mg/kg

Vehicle : other: corn oil

Route of administration : gavage Exposure time : 48 hour(s)

Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :

Half-lives

1st: 2nd: 3rd:

Toxic behaviour : Deg. product :

Method : other: EPA test rule study

Year

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female F344 rats (7 wk old; n=4/sex) were given a single oral treatment of 1 or 100 mg/kg bwt 14C-labelled PDC

(50 or 500 uCi/kg bwt, respectively) in corn oil. A third group received 7 daily oral doses of 1 mg/kg bwt

non-radiolabeled PDC, followed by a single oral dose of 1 mg/kg bwt 14C-labeled PDC on day 8. Food was withdrawn 16 hr

mg/kg bwt 14C-labeled PDC on day 8. Food was withdraw prior to dosing, and returned 4 hr post-treatment. The

animals were housed in glass metabolism cages, and urine, feces and expired carbon dioxide and volatile substances collected for up to 48 hr post-dosing. The concentration of 14C in plasma (indwelling jugular cannula) was determined repeatedly during post-dosing period. Samples of body tissues (blood, bone, brain, liver, kidneys, fat, gonads, lung, heart, skeletal muscle, spleen, skin and carcass)

were analys ed for radioactivity at 48 hr.

Test samples

The unlabelled material was 99.9% pure. The labelled material was 97% pure, had a specific activity of 17

mCi/mmol and was uniformly labelled on a single carbon atom.

Analytical methods

Total radioactivity in urine (plus distilled water cage rinse) and blood (plasma) was quantified by liquid scintillation counting (LSC). Feces were processed using a sample oxidiser, the released carbon dioxide trapped in 1-methoxy-2-propanol:monoethanolamine (7:3) and radioactivity determined by LSC; exhaled carbon dioxide was quantified in an analogous manner. Exhaled volatile compounds were trapped on activated charcoal, desorbed (hexane) and subject to LSC.

Major urinary metabolites were separated by reverse phase HPLC both before and after acid hydrolysis. Metabolite identification was by full-scan chemical ionization-GC/MS.

Kinetic analysis

The data were fitted to a one compartment open pharmacokinetic model with zero-order input rate, and half-lives calculated, using the SIMUSOLV computer programme (Mitchell and Gauthier Associates, Inc, Concord, MA).

Statistical analysis

ANOVA and Tukeys test were applied to the data.

Recovery of radioactivity

Results for the recovery and excretion of radioactivity following oral administration of PDC are given in Attachment 5.0a.

Single dose:

In summary, urine (46-52%) and expired CO2 (23-36%) accounted for over two-thirds of the dose, with smaller amounts present in tissues and carcass (7-11%) and faeces (7-8%). Less than 3% of the dose was present in cage washings. Exhaled volatiles accounted for 0.3-1.1% of the dose in animals given 1 mg/kg bwt, and 10-16% of the administered radioactivity in high dose animals. Overall, 100-107% of the radiolabel was recovered.

The proportion of the dose excreted as CO2 was significantly lower in rats given 100 mg PDC/kg bwt relative to that for rats given 1 mg/kg; conversely exhalation of radioactivity in the volatile fraction was significantly greater than in the low dose group. While the pattern of excretion was generally similar in males and females, statistical analysis indicated less of the dose was excreted as CO2 and more in the urine in females compared to males.

Multiple doses:

While the overall pattern of excretion and recovery of 14C-label was comparable to that seen in animals given a single treatment, there was a statistically significant decrease (approx. 10%) in percentage recovered in urine from the repeat dose animals. Elimination of 14C-CO2 was slightly but significantly increased in the repeat dose group for females.

Analysis of tissues

Radioactivity was distributed among all the tissues examined. The liver contained the highest amount (0.2-0.4% of the dose /g wet weight), with generally 0.1% or less

99/99

Result

present in the other organs. There were no obvious differences in tissue distribution between the sexes or the different dosing regimens.

Timecourse for elimination

Elimination was greatest over the first 24 hr post-dosing, with negligible amounts eliminated during the 24-48 hr period. In urine, 35-50% of the dose was recovered during the first 24 hr, with trace amounts (1-2%) excreted subsequently. Comparative figures for exhaled carbon dioxide were 21-33% and 2-3%, and 5-7% and 0.5-1.0% for faeces (at 0-24 and 24-48 hr, respectively).

In plasma, the highest concentration of 14C in both sexes was found at 4 hr post-dosing, with 0.3-0.4 ug eq/g plasma present in low dose animals and 24-28 ug eq/g plasma in animals given 100 mg/kg bwt. Corresponding AUCs were 4.2-5.4 ug g^1 and 351-368 ug g^1, respectively. These results suggest that levels in plasma were slightly less than dose-proportionate (perhaps indicating saturation of biotransformation at the higher dose).

There were no obvious differences in timecourse for elimination between the sexes or the different dosing regimens used in the study.

Metabolites

Approx. 82% of the radioactivity present in the exhaled volatile fraction was unchanged PDC. No unchanged PDC was present in urine. Three n-acetylcysteine conjugates were detected in urine, (N-acetyl-S-(2-hydroxypropyl)-L-cysteine,

N-acetyl-S-(2-oxopropyl)-L-cysteine and

N-acetyl-S-(2-carboxyethyl)-L-cysteine). These accounted for 10%, 14% and 2% of the dose given to the 100 mg/kg bwt animals, respectively. Attempts to identify three other HPLC

peaks were unsuccessful.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document

Conclusion

Attachment 5.0a.doc

Urine and exhaled carbon dioxide were the principle routes for excretion of PDC in male and female rats after single or repeated oral administration. The pathway leading to CO2 is quantitatively less important at higher doses. The majority of radioactivity was excreted within 24 hr, with little or

no unchanged PDC present.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (162)

In Vitro/in vivo : In vivo : Metabolism

Species

Number of animals

Males :

Females : 2

Doses

Males

Females : 100 mg/kg

Vehicle : other: corn oil

Route of administration : gavage Exposure time : 24 hour(s)

Product type guidance

Decision on results on acute tox. tests : Adverse effects on prolonged exposure :

Half-lives

1st: 2nd: 3rd:

Toxic behaviour

Deg. product

Method : other: EPA test rule study

Year

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Two female F344 rats (12 wk old) were administered deuterated PDC (D6-PDC, 100 mg/kg bwt) to examine the mechanism of formation of urinary metabolites. After

treatment the animals were housed in glass metabolism cages and urine collected for 24 hr. The test material contained an average of 5.9 deuterium atoms, with less than 1%

unlabelled material present.

Analysis

Urine samples were derivatized twice (ethereal diazomethane and N,O-bis(trimethylsilyl)trifluoroacetamide) and analysed

by GC-MS.

Result: Three mercapturic acids were identified as urinary

metabolites of PDC:

Metabolite I

2-hydroxypropylmercapturate (containing 3 deuterium atoms);

Metabolite II

2-oxopropylmercapturate (containing 3 deuterium atoms);

Metabolite III

1-carboxyethylmercapturate (containing 4 deuterium atoms);

Based on the number of deuterium atoms present, the authors propose that PDC undergoes oxidation, either prior to or following conjugation with glutathione to give Metabolite II and Metabolite III. Enzymatic reduction of Metabolite II

gives Metabolite I.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Conjugation with glutathione is an important pathway for the

metabolism of PDC in vivo.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (162)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50

Value : = 2200 mg/kg bw

Species : rat

Strain : other: Carforth-Wistar

Sex : male/female

Number of animals : 5 Vehicle : Doses :

Method :

Year : 1969 **GLP** : no

Test substance : as prescribed by 1.1 - 1.4

Method : The acute oral toxicity of PDC was determined in groups of

non-fasted Carworth-Wistar rats (males and females, 4-5 wk

old, non-fasted).

PDC was administered undiluted, and doses were arranged in a

logarithmic series and differed by a factor of two.

Animals were onserved for 14 d post-treatment, and the LD50 calculated using the methods of Thompson (Bacteriol. Rev. (1947) 11, 115) and Weil (Biometrics (1952) 8, 249). The

result is presented as the mean and SD.

Result : Acute oral LD50 = 1.9 + /- 0.2 ml/kg (mean and SD)

This is equivalent to 2200 mg/kg bw, based on a density of 1.155 g/ml [Source: MacKay et al (1993) Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for

Organic Chemicals, Vol III, p479]

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : 1,2-Dichloropropane. **Reliability** : (2) valid with restrictions

Early (pre-guideline) study. Methods and results briefly

reported. Generally acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (163) (164)

Type : LD50

Value : = 2890 mg/kg bw

Species : r Strain : Sex :

Number of animals

Vehicle : other: aqueous emulsion in Traganth

Doses : 2-20%

Method :

Year : 1965 **GLP** : no

Test substance : as prescribed by 1.1 - 1.4

Method : Rats (strain, number and sex not specific) were given a

single oral treatment with 2-20% PDC, as an aqueous emulsion in Traganth. Animals were observed for 7 d post-dosing, prior to necropsy (macroscopic examination). The LD50 was calculated using the method of Litchfield and Wilcoxon.

Result : Clinical signs were reported as apathy and orange-coloured

urine.

The acute oral LD50 was 2.5 ml/kg (equivalent to 2890 mg/kg bwt, based on a density of 1.155 g/ml [Source: MacKay et al

(1993) Fate of Organic Chemicals, Vol III, p479]). The 1,2-Dichloropropane ICCA/HPV Consortium

Source : The 1,2-Dichloropropane ICCA/HPV Consort

Reliability : (4) not assignable

Early (pre-guideline) study. Methods and results briefly

reported.

Flag : Critical study for SIDS endpoint

25.10.2004 (165)

Type : LD50

Value : = 1942 mg/kg bw

Species : rat Strain :

Sex :

Number of animals : Vehicle : Doses :

Method : other: Acute Oral Toxicity

Year : 1959 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (166)

Type : LD50

Value : ca. 460 mg/kg bw

Species : rat

Strain

Sex :

Number of animals : Vehicle :

Doses

Method : other: BASF-Test

Year : 1981 GLP : no Test substance : other TS

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : Described as "1,2-dichloropropane raw OE". No information

available on chemical composition, purity or presence of

other acutely toxic substances.

Reliability : (3) invalid

25.10.2004 (167)

Type : LD50

Value : ca. 1000 mg/kg bw

Species: ratStrain:Sex:

Number of animals : Vehicle : Doses :

Method : other: BASF-Test

Year : 1978 GLP : no Test substance : other TS

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Test substance : Described as "1,2-dichloropropane raw". No information

available on chemical composition, purity or presence of

other acutely toxic substances.

Reliability : (3) invalid

29.02.2004 (168)

Type : LD50

Value : = 860 mg/kg bw

Species : mouse

Strain :

Number of animals

Vehicle

Doses

Method : other: Acute Oral Toxicity

Year : 1986 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (169)

Type : LD50

Value : = 960 mg/kg bw

Species : mouse

Strain

Sex

Number of animals ::
Vehicle ::

Doses

Method : other: Acute Oral Toxicity

Year : 1982 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (170)

Type : LD50

Value : = 2000 mg/kg bw Species : guinea pig

Strain

Sex

Number of animals Vehicle

Doses

Method : other: Acute Oral Toxicity

Year : 1989
GLP : no data
Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (171)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50 **Value** : = 2000 ppm

Species : rat

Strain : Sherman
Sex : male/female

Number of animals : 6
Vehicle :

Doses

Exposure time : 4 hour(s)

Method

Remark

Source

Year : 1949 **GLP** : no

Test substance: as prescribed by 1.1 - 1.4

Method : Six male or female Sherman rats (approx. 100 - 150 g) were

exposed to PDC vapor (nominal concentrations up to 2000 ppm)

for 4 hr or 8 hr, then observed for a 14 day follow-up

period.

The test atmosphere was generated by passing air (2.5 l/min) through a fritted glass disc immersed in liquid PDC. The resulting vapour-laden stream was mixed with fresh air to produce a series (log base 2) of exposure concentrations. The reported values are nominal (based on weight of material

evaporated) and not verified analytically. Conversion factor: 1 ppm = 4.70 mg/l

Result : Results from a preliminary study, summarised in tabular

form, indicate that there was 33-67% mortality following 4 hr exposure to 2000 ppm PDC (equivalent to 9.4 mg/l).

There were 3/6 deaths in the definitive study following an 8

hr exposure to this same concentration.

Thus the same extent of mortality was observed in rats exposed to PDC vapor for 4 hr or 8 hr. Since the longer exposure was not more hazardous than the shorter expoure, it is concluded that these results most likely reflect the 4

hr acute toxicity of 1,2-dichloropropane in the rat. The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : The 4 hr inhalation LC50 for PDC in the rat is 2000 ppm (9.4

mg/l).

Reliability : (2) valid with restrictions

Early (pre-guideline) study, generally well documented and

acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (172) (164)

Type : LC50 **Value** : > 2200 ppm

Species : rat

Strain : Sprague-Dawley

Sex : no data Number of animals : 33

Vehicle

Doses : 2200 ppm Exposure time : 7 hour(s)

Method : Year :

GLP : no Test substance : no data

Method : Thirty three adult rats (bwt 150 - 200 g) were exposed once

to a 2200 ppm (nominal) PDC vapour for 7 hr.

The concentration of PDC in the exposure chamber was calculated from measurements of the weight of solvent

ld 78-87-5 5. Toxicity Date 14.12.2004

> volatilised and the rate of air flow through the chamber. This was compared with the analysed content of PDC in a sample of chamber air, quantified using thermal decomposition and estimation of inorganic chloride.

Groups of 3-5 animals taken for necropsy on days 0, 1, 2, 4, 7, 9 and 14 days post-exposure, and subject to macroscopic evaluation. Tissue sections were prepared from adrenals, heart, liver, kidney and subject to microscopic examination. Three unexposed rats served as controls.

1 ppm = 4.70 mg/m3

Remark

Result Two rats died shortly after exposure, while the remainder survived until scheduled necropsy. (Advanced autolysis precluded microscopic evaluation of tissues from the

decedents.)

Slight visceral congestion and fatty liver were the main macroscopic changes present.

Microscopic examination of the liver revealed marked-to-moderate, midzonal-to-diffuse, fine droplet fatty degeneration with centrilobular necrosis in all animals sacrified 24 hr post-exposure. Some necrotic liver cells were also present in 3/5 rats 48 hr post-treatment, and 1/3 rats at 4 days. Glycogen depletion was present 24-48 hr post-exposure, while deposition of hemosiderin in Kupffer cells was present from day 4 onwards. Livers of rats sacrificed 2 days after exposure to PDC showed some increase in occurrence of scattered mitotic figures.

Fine droplets of fat were observed in convoluted tubules and thick portions of the loop of Henle of 4/5 rats at day 1 post-exposure and 2/5 on day 2, with minimal fatty change in 3/5 rats at day 7.

The amount of fat in the adrenal cortex showed a slight-to-moderate decrease in animals necropsied immediately and 24 hr post-exposure.

Interstitial pneumonia was present occasionally in all

groups, including controls.

Source The 1,2-Dichloropropane ICCA/HPV Consortium Conclusion

Under the conditions of the study, the inhalation LC50 for

PDC in the rat was >2200 ppm (7 hr exposure).

Treatment-related changes appeared limited primarily to

liver.

Reliability (2) valid with restrictions

Early (pre-guideline) study, generally well documented and

acceptable for assessment.

Critical study for SIDS endpoint Flag

25.10.2004 (173)

Type : LC50 Value > 2200 ppm Species guinea pig Strain no data Sex no data Number of animals 33 Vehicle

Doses

Exposure time 7 hour(s)

Method

Year :

GLP : no Test substance : no data

Method : Thirty three adult guinea pigs (bwt 600 - 800 g) were

exposed to a 2200 ppm (nominal) PDC vapour for 7 hr.

The concentration of PDC in the exposure chamber was calculated from measurements of the weight of solvent volatilised and the rate of air flow through the chamber. This was compared with the analysed content of PDC in a sample of chamber air, quantified using thermal

decomposition and estimation of inorganic chloride.

Groups of 2-5 animals taken for necropsy on days 0, 1, 2, 4, 7, 9, 11, 14, 16 and 21 after treatment, and subject to macroscopic evaluation. Tissue sections were prepared from

macroscopic evaluation. Tissue sections were prepared from adrenals, heart, liver, kidney and subject to microscopic examination. Three unexposed guinea pigs served as controls.

Remark : 1 ppm = 4.70 mg/m3

Result : There were no premature deaths during the study. At necropsy, many animals showed slight visceral congestion and

fatty change in the liver, while the cut surface of the adrenal glands showed a hemorrhagic central portion.

Microscopic examination revealed small-to-moderate amounts of fat in the heart, liver and kidney of exposed animals sacrificed immediately after treatment.

Exposed animals showed a reduction in liver glycogen on day 0 and day 1 post-treatment, a normal amount at day 2 then a marked increase from day 4 onwards. Hepatocytes in affected animals were swollen with pale, vaculoated cytoplasm, especially in the centrilobular region.

Histopathological changes in adrenal tissue included thickening, vacuolation, hemorrhage increased occurence of mitotic figures and necrosis of the cortex during the first week post-treatment. These changes began to resolve during the second week post-exposure and adrenal tissue from two out of three guinea pigs sacrificed on day 21 appeared normal. Changes in the medulla included congestion, oedema, white cell infiltration and occasional necrotic cells up to day 7, but these tended to have resolved by day 9. Deposits of fat and hemosiderin were present in connective tissue

: The 1,2-Dichloropropane ICCA/HPV Consortium

surrounding the medulla at day 21.

Conclusion: Under the conditions of the study, the inhalation LC50 for

PDC in the guinea pig was >2200 ppm (7 hr exposure). Treatment-related changes appeared limited to primarily to

the adrenal gland.

Reliability : (2) valid with restrictions

Early (pre-guideline) study, generally well documented and

acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (173)

 Type
 : LC50

 Value
 : = 14 mg/l

 Species
 : rat

 Strain
 :

 Sex
 :

Source

Number of animals : Vehicle : Doses :

Exposure time : 8 hour(s)

Method : other: Acute Inhalation Toxicity

Year : 1959 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (166)

 Type
 : other: IRT

 Value
 : = ppm

 Species
 : rat

Strain Sex

Source

Sex Number of animals

Vehicle

Doses

Exposure time : minute(s)

Method : other: not specified

Year : 1978 GLP : no Test substance : other TS

Remark: The exposure of 12 rats to a saturated atmosphere of

1,2-dichloropropane at 20 degrees C for 3 minutes caused no

lethality. All rats (groups of 6) died when they were exposed to 1,2-dichloropropane for 10 or 15 minutes. The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : "1,2-dichloropropane crude"

Reliability : (3) invalid

Other Test Material

25.10.2004 (168)

 Type
 : other: IRT

 Value
 : = ppm

 Species
 : rat

 Strain
 :

Sex :
Number of animals :
Vehicle :
Doses :

Exposure time : minute(s)

Method : other: not specified

Year : 1965 **GLP** : no

Test substance : as prescribed by 1.1 - 1.4

Remark: The exposure of 12 rats to a saturated atmosphere of

1,2-dichloropropane at 20 degrees C for 3 minutes caused no

lethality. Three rats died after exposure for 10 minutes .

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

rel iability.

26.10.2004 (165)

Type : other: LT0 **Value** : = 6.9 mg/l

Species : rat Strain :

Sex

Number of animals :
Vehicle :
Doses :
Exposure time :

Method : other: Acute Inhalation Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark : LTO = time within which none of the tested animals died: > 7

hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type : other: acute inhalation toxicity

Value : = 10.34 mg/l

Species: ratStrain:Sex:Number of animals:

Vehicle :
Doses :

Exposure time : 7 hour(s)

Method : other: Acute Inhalation Toxicity

Year : 1942 GLP : no data Test substance : no data

Remark: Four days after exposure, an increased

sedimentation of hemosiderin was observed in von Kupffer's

cells centrilobularly located. Mortality: 3/33.

Sprague-Dawley were dissected and centrilobular necrosis, fatty degeneration and a decreased glycogen content in the liver were found after being exposed to 1,2-dichloropropane

for 24 hours.

The animals, exposed to 1,2 dichloropropane were dissected immediately after the exposure or 7 days later. They showed

no substance-caused damage to the liver.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the I UCLID entry to determine

reliability.

26.10.2004 (173)

Type : LC50
Value : = 2.256 mg/l
Species : mouse

Strain :

Sex :
Number of animals :
Vehicle :
Doses :

Exposure time : 10 hour(s)

Method : other: Acute Inhalation Toxicity

ld 78-87-5 5. Toxicity Date 14.12.2004

Year 1968 **GLP** no data **Test substance** no data

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (175)

Type other Value = 4.6 mg/l**Species** mouse

Strain Sex

Number of animals Vehicle **Doses**

Exposure time 4 hour(s) Method other Year 1978 **GLP** no data **Test substance** no data

Remark Measured parameters were SGOT, SGPT, glucose-6-phosphatase

> and ornithine carbamoyltransferase enzymes in the serum of male rats following a single 4-hour inhalation exposure at a concentration of 4620 mg/m3. A significant increase in enzyme activities was observed for SGOT, SGPT and ornithine

carbamovltransferase at 24 and 48 hours.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (176)

Type other: LT0 Value = 4.4 mg/l**Species** mouse

Strain

Sex

Number of animals Vehicle **Doses Exposure time**

Method : other: Acute Inhalation Toxicity

Year 1946 **GLP** no data **Test substance** no data

Remark : LT0 = time within which none of the tested animals died:

approx. 1 hour

Source The 1,2-Dichloropropane ICCA/HPV Consortium

(4) not assignable Reliability

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type other: LT100 Value = 4.4 mg/l**Species** mouse

Strain

Sex :
Number of animals :
Vehicle :
Doses :
Exposure time :

Method : other: Acute Inhalation Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark : LT100 = time within which all of the tested animals died:

approx. 4 hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

 Type
 : other: LT50

 Value
 : = 3.389 mg/l

 Species
 : mouse

Strain

Sex :

Number of animals : Vehicle : Doses :

Exposure time : 8.3 hour(s)

Method : other: Acute Inhalation Toxicity

Year : 1968
GLP : no data
Test substance : no data

Remark : LT50 = time within which 50% of the tested animals died Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (175)

Type : other: see remark
Value : = 6.5 mg/l
Species : mouse

Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Exposure time : 2 hour(s)

Method : other: Acute Inhalation Toxicity

Year : 1946 GLP : no data Test substance : no data

Remark : Mortality: 3/10

Symptoms: fatty degeneration in liver and kidney as well as

centrilobular necrosis of the liver.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type : other: LT0
Value : = 6.9 mg/l
Species : rabbit

Strain :

Sex :

Number of animals
Vehicle
Doses

Exposure time

Method : other: Acute Inhalation Toxicity

Year : 1946 GLP : no data Test substance : no data

Remark : LTO = time within which none of the tested animals died: > 7

hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type: other: LT0Value: = 4.4 mg/lSpecies: dog

Strain : Sex :

Number of animals : Vehicle : Doses : Exposure time :

Method : other: Acute Inhalation Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark : LTO = time within which none of the tested animals died: > 7

hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type: other: LT0Value: = 6.9 mg/lSpecies: guinea pig

Strain

Sex :

Number of animals : Vehicle : Doses :

Exposure time :

Method : other: Acute Inhalation Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark: LTO = time within which none of the tested animals died: > 7

hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50

Value : = 10100 mg/kg bw

Species : rabbit

Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :

Year : 1962
GLP : no
Test substance : no data

Method: PDC was applied to clipped skin of male albino rabbits (2.5

- 3.5 kg, n=4 per treatment) under occlusion for 24 hr. The animals were immobilised during expoure, then returned to

their cages and observed for 14 days.

Result : An LD50 of 8.75 ml/kg bw was reported. This is equivalent to

10,100 mg/kg bw, based on a density of 1.155 g/ml [Source:

MacKay et al (1993) Illustrated Handbook of

Physical -Chemical Properties and Environmental Fate for

Organic Chemicals, Vol III, p479]

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, the dermal LD50 for PDC

in male rabbits was 8.75 ml/kg bw (10100 mg/kg bw).

Reliability : (2) valid with restrictions

Early (pre-guideline) study, generally well documented and

acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (163)

Type : LD50

Value : > 2000 mg/kg bw

Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses : rat

Method : other: BASF-Test

Year : 1981 GLP : no Test substance : other TS

Remark: no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : "1,2-dichloropropane crude OE"

Reliability : (3) invalid

Other test material

25.10.2004 (177)

Type : LD50

Value : = 10115 mg/kg bw

Species : rabbit

Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Method : other: Acute Dermal Toxicity

Year : 1962 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (164)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50

Value : = 1100 mg/kg bw

Species: ratStrain:Sex:Number of animals:

Vehicle :
Doses :
Route of admin. : i.p.

Exposure time : 1.p.

Method : other: Acute Intraperitoneal Toxicity

Year : 1989 GLP : no data

Test substance : other TS: purity = 97 %

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (178)

Type : LD50

Value : ca. 230 mg/kg bw

Species: ratStrain:Sex:

Number of animals : Vehicle : Doses :

Route of admin. : i.p.

Exposure time :

Method : other: BASF-test

Year : 1965 GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Remark: no additional information

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (165)

Type : LD50

Value : = 700 - 2000 mg/kg bw

Species: mouse

Strain

Sex

Number of animals : Vehicle : Doses :

Route of admin. : i.p.

Exposure time

Method : other: BASF-test

Year : 1981 GLP : no Test substance : other TS

Remark: no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : "1,2-dichloropropane crude OE"

Reliability : (3) invalid

Other test material

25.10.2004 (177)

Type : LD50

Value : = 316 - 4640 mg/kg bw

Species : mouse

Strain :

Number of animals : Vehicle : Doses :

Route of admin. : i.p.

Exposure time

Method : other: BASF-test

Year : 1978 GLP : no Test substance : other TS

Remark: no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : "1,2-dichloropropane crude"

Reliability : (3) invalid

Other test material

25.10.2004 (168)

5.2.1 SKIN IRRITATION

Species: rabbitConcentration: undilutedExposure: SemiocclusiveExposure time: 4 hour(s)

Number of animals : 3 Vehicle :

PDII

Result : slightly irritating
Classification : not irritating

Method

Year : 1982 GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : OECD Guideline 404. White Vienna rabbits (2 male, mean bwt

3.26 kg; 1 female bwt 2.89 kg) were used.

0.5 ml DCP was applied to a 2.5 cm x 2.5 cm piece of gauze which was held in contact with clipped rabbit skin (upper back or flank) under semi-occlusive conditions for 4 hr.

After removal of the patch, the application site was

cleaned with lutrol/water (1:1) and skin reactions recorded

at 24 hr, 48 hr, 72 hr and 8 d post-treatment.

Result : Individual reactions at 24 hr:

Redness 2, 2, 2 Oedema 1, 1, 1

Individual reactions at 48 hr:

Redness 2, 1, 1 Oedema 0, 0, 0

Individual reactions at 72 hr:

Redness 1, 1, 1 Oedema 0, 0, 0

Individual reactions at 8 d

Redness 1, 0, 0 Oedema 0, 0, 0

Flaking skin at application site in all animals
The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Slightly irritating to skin.
Reliability : (2) valid with restrictions

Guideline study

Flag : Critical study for SIDS endpoint

25.10.2004 (179)

Species : rabbit

Concentration :

Exposure :

Exposure time :

Number of animals :

Vehicle :

PDII :

Source

Result : not irritating

Classification

Method : other: Acute Dermal Irritation

Year : 1962 GLP : no data Test substance : no data

Remark : Dermal application on shaved abdominal skin (nonocclusive);

effect time: 24 hours

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (164)

Species : rabbit

Concentration :

Exposure :

Exposure time :

Number of animals :

Vehicle PDII

Result corrosive

Classification

Method other: BASF-Test

Year 1981 **GLP** : no Test substance other TS

Remark "1,2-dichloropropane crude OE"

occlusive application; no additional information.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (3) invalid

Other test material

25.10.2004 (177)

Species rabbit

Concentration

Exposure

Exposure time

Number of animals

Vehicle

PDII

Result slightly irritating

Classification

Method other: BASF-Test

Year 1982 **GLP** Test substance other TS

Remark "1,2-dichloropropane crude OE"

Semiocclusive application; no additional information.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (3) invalid

Other test material

25.10.2004 (180)

rabbit Species

Concentration Exposure **Exposure time Number of animals** Vehicle PDII

Result highly irritating

Classification

Method other: BASF-Test

Year 1978 **GLP** no **Test substance** other TS

Remark "1,2-dichloropropane crude"

no additional information.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

(3) invalid Reliability

Other test material

25.10.2004 (168)

5.2.2 EYE IRRITATION

ld 78-87-5 5. Toxicity Date 14.12.2004

Species rabbit Concentration undiluted Dose .05 ml **Exposure time** unspecified

Comment

Number of animals Vehicle

Result irritating

Classification Method

Year 1965 GLP

no data **Test substance** as prescribed by 1.1 - 1.4

Result Slight redness and oedema with slight opacity were present 1

hr post-treatment, with marked redness and odema and slight

opacity at 24 hr. All signs had resolved 8 d post-treatment.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion Irritating to the eye. Reliability (2) valid with restrictions

Early (pre-guideline) study, generally well documented and

acceptable for assessment.

Flag Critical study for SIDS endpoint

25.10.2004 (165)

Species rabbit

Concentration Dose **Exposure time** Comment **Number of animals**

Vehicle

Result slightly irritating

Classification

Method other: Eye Irritation

Year 1962 **GLP** no : **Test substance** no data

Remark Application of 0.5 ml undiluted 1,2-dichloropropane;

irritation index 2 of 10 maximum

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (181)(164)

Species rabbit

Concentration Dose

Exposure time Comment **Number of animals** Vehicle

Result irritating

Classification

Method other: BASF-Test

Year 1981 GLP no Test substance other TS

Remark "1,2-dichloropropane crude OE"

no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (3) invalid

Other test material

25.10.2004 (182)

Species : rabbit

Concentration

Dose

Exposure time Comment

Number of animals Vehicle

Result : irritating

Classification

Method : other: BASF-Test

Year : 1978 GLP : no Test substance : other TS

Remark : "1,2-dichloropropane crude"

no additional information.

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

Reliability : (3) invalid

Other test material

11.10.2004 (168)

Species : rabbit

Concentration :

Dose :

Exposure time

Comment

Number of animals

Vehicle

Result : irritating

Classification

Method : other: BASF-Test

Year : 1965 **GLP** : no

Test substance : as prescribed by 1.1 - 1.4

Remark: no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (165)

5.3 SENSITIZATION

Type : Mouse local lymphnode assay

Species : mouse

Number of animals :

Vehicle : other: acetone olive oil Result : not sensitizing

Classification

Method : other: OECD 429 (2002); U.S. EPA OPPTS 870.2600 (2003)

Year : 2003

GLP : yes

Test substance :

Method

: Range-finding Test

Selection of the upper-dose level for the definitive study was based upon results from an irritation range-finding test where 80%, 60%, 40%, 20%, or 10% v/v PDC in acetone:olive oil (AOO) was applied to each ear of female mice (1 mouse /dose) on two consecutive days. No appreciable ear swelling or erythema were noted and 80% v/v was chosen as the highest dose.

Main study (LLNA)

Groups of six female BALB/c mice (approximately 18 g, 8 weeks old) received topical applications (25 ul/ear, total 50 ul/mouse) of 5%, 20% or 80% propylene dichloride (PDC) in AOO on three consecutive days. A positive control group was treated with 30% a-hexyl cinnamaldehyde (HCA), a recognized skin contact allergen, diluted using AOO.

On day 6, all mice received a 250 µl intravenous injection via the lateral tail vein containing 20 µCi of 3H-thymidine (specific activity 2Ci/mmol; Amersham code TRA310) diluted in phosphate buffered saline (PBS). Approximately five hours later, the mice were sacrificed and the auricular lymph nodes (located at bifurcation of the jugular veins) excised, combined for each mouse and placed in PBS.

A single cell suspension of lymph node cells was prepared by gentle mechanical disaggregation using a tissue homogenizer. The cells were washed using PBS and suspended in 5% trichloroacetic acid (TCA); suspended precipitates were centrifuged and the pellets reconstituted in 1 ml of 5% TCA prior to transfer to a scintillation vial containing 10 ml of Aquasol-2 scintillation cocktail. Tubes used for suspending the pellets were rinsed using two additional 2-ml aliquots of water and the rinses were added to the scintillation vials. The radioactivity in each precipitate (representing two lymph nodes from one animal) was measured using a B-scintillation counter and reported as disintegrations per minute (dpm) per mouse.

Interpretative criteria

In addition to the application of statistical methods, sensitization potential was further determined by the magnitude of any lymphocyte proliferative response in relation to vehicle controls. A stimulation Index (SI) of = or > 3 (i.e. 3-fold or greater prolife ration than control animals) was considered indicative of a potential for dermal sensitization.

Statistical methods

Comparisons of dpm values for treated vs. control groups were done by Dunnett's t-test when ANOVA results suggested differences. The alpha level at which all tests were conducted was 0.05.

Result

PDC did not demonstrate any lymph node cell proliferation response, nor any LLNA results (dpm and SI) consistent with dermal sensitization as the lymph nodes draining the area of topical application did not demonstrate a proliferative response equal to or greater than the 3x threshold. SI values were consistently around 1.0 (equivalent to vehicle

ld 78-87-5 5. Toxicity Date 14.12.2004

controls) at all doses tested:

Proliferative response

Control A (mean and SD)

В 5% 20% С 80% D

Proper conduct and responsiveness of the test was confirmed in animals treated with 30% HCA (positive control group) where proliferation (SI) was 14-fold greater than that of vehicle controls.

Because the SI values for 5, 20, and 80% PDC were all below 3, an EC3 value could not be determined. On the basis of these results, PDC did not demonstrate any contact sensitization potential.

Source The 1,2-Dichloropropane ICCA/HPV Consortium Conclusion 1,2 dichloropropane did not stimulate proliferation of

> lymphocytes in auricular lymph nodes from mice treated with up to 80% PDC in AOO on 3 consecutive days. It was concluded that PDC was not a sensitiser under the conditions of this

assay.

Reliability (1) valid without restriction

GLP guideline study.

25.10.2004 (183)

Type Patch-Test Species human

Number of animals

Vehicle petrolatum Result ambiguous

Classification Method

Year 1989 **GLP** no Test substance no data

Method Subjects and symptoms

> The test subjects were 10 workers (painters, metal workers) with exposure to mixed solvents, including preparations containing 10-40% 1,2-dichloropropane (analysis by GLC, no details presented). Reported symptoms included itchy erythematous, odematous lesions on the fingers and dorsa of the hands, with scaling and fissuring of the palms in 2 individuals. The patients were assessed during the period 1985-1988. 120 control subjects were included in the

investigation (no further details provided).

Patch testing

Patch tests were carried out "according to internationally accepted methods" (no further details provided) using Porotest on Scanpor, with readings made according to ICDRG recommendations (no further details provided). PDC (1%, 2%, 5%, 10%, 20%) and other product constituents (resins, solvents, mineral oils, perchloroethylene,

trichloroethylene) were tested in addition to the European

standard series (Hermal-Trolab).

Comment: no information is provided on the origin or purity of the PDC used during the challenge phase of this study.

Statistical methods

None applied (observational study).

Result : Control subjects

No response to PDC was noted in 118 of the control subjects; slight erythema was present in the two remaining control individuals after challenge with 20% PDC in petrolatum. With the exception of a single positive reaction to methyl acrylate, no positive response was noted toward the other substances included in this study (no further details provided).

Test subjects

Skin reactions were elicited in all 10 subjects after patch testing with PDC, although not all responded for all tests.

Responses were reported as follows:

1% PDC: 1 score + ; 1 score ++ ; 4 score - ; 4 not

tested

2% PDC: 5 score +; 2 score +++; 3 not tested 5% PDC: 4 score +; 4 score ++; 2 score +++; 10% PDC: 1 score +; 7 score +++; 2 score ++++; 20% PDC: 4 score +++; 4 score ++++; 2 not tested

A biopsy was performed on one subject (5% challenge site; skin response = score ++). Spongiosis, oedema and early vesiculation of the epidermis was present with perivascular

lymphocytic infiltrate in the dermis.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion : The authors conclude that 1,2 dichloropropane w

The authors conclude that 1,2 dichloropropane was responsible for skin reactions observed in this group of workers. Given the dearth of methodological and results detail presented in the publication, including no information on the origin or purity of the sample used during the challenge phase, and since the structure of PDC contains no obvious chemical groups with a potential to react with cellular components, this evidence is considered

equivocal.

Reliability : (4) not assignable

Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown

reliability.

Flag : Critical study for SIDS endpoint

25.10.2004 (184)

Type : Patch-Test Species : human

Number of animals Vehicle

Result : Classification : Method :

Year : 1981

GLP : no
Test substance : other TS

Remark: Two female workers reported cases of recurrent dermatitis

and were tested with 1% 1,2-dichloropropane and other

substances present in their workplaces.

One individual had a reaction to several substances

including PDC.

A second individual demonstrated low grade responses to chromate and PDC. This individual reported that initial

symptoms were noted on her feet and one incident of a rash under a leather watch strap. This may indicate a reaction to chromates which are sometimes used in the tanning process of leathers.

The PDC used for the patch tests was of technical grade, which could comprise other components and/or impurities.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance : No information available. **Reliability** : (4) not assignable

Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown

reliability.

25.10.2004 (185)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic

Species : rat

Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13 wk
Frequency of treatm. : 5 d/wk
Post exposure period : None

Doses : 0, 60, 125, 250, 500 or 1000 mg/kg bw/d

Control group : yes, concurrent vehicle

NOAEL : = 250 mg/kg bw

LOAEL : = 500 mg/kg bw

Method: other: standard NTP methodology

Year : 1986 GLP : ves

Test substance: as prescribed by 1.1 - 1.4

Method : Groups of 10 m ale and 10 female F344 rats (age 7 -8 wk at

start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 60, 125, 250, 500 or 1000 mg/kg bw/d 5 d/wk for 13 wk. The animals were group housed and observed daily for clinical signs and twice daily for mortality. Animals judged to be moribund were taken to necropsy. Each animal was given a detailed weekly examination, including palpation for tissue masses or

swelling. Body weights were taken weekly.

Necropsies were performed on all surviving animals at the end of the treatment period. A comprehensive range of tissues were sampled and preserved, and those from the controls, 500 mg/kg and 1000 mg/kg groups subject to

microscopic examination.

The concentration of test article in the dosing solutions

was verified using GC -FID.

Result : GC analysis of the dosing solutions demonstrated that the

achieved concentration was 95 - 100% of target.

All male and female rats given 1000 mg/kg bw/d and 5/10 males from the 500 mg/kg bw group died before necropsy. All animals from the other treatment groups survived until study termination. Final mean body weights were decreased 16% in

male and 8% in females given 500 mg/kg bw/d.

The liver was the only organ to be affected by treatment, with centrilobular congestion present in 5/10 males and 2/10 females given 1000 mg/kg bw/d. Hepatic fatty change and centrilobular necrosis were observed in 2/10 females from

the 1000 mg/kg bw/d group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Under the conditions of the study, the sub-chronic NOEL for

PDC in the rat was 250 mg/kg bw/d, based upon mortality and lower body weight in males, and lower body weight with no histopathological involvement in females, given 500 mg/kg

bw/d.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Chronic Species : rat

Sex: male/femaleStrain: Fischer 344Route of admin.: gavageExposure period: 103 wkFrequency of treatm.: 5 d/wk

Post exposure period

Doses : males 0, 62 or 125 mg/kg bw/d; females 0, 125 or 250 mg/kg bw/d

Control group : yes, concurrent vehicle
NOAEL : = 62 - 125 mg/kg bw
LOAEL : = 125 - 250 mg/kg bw

Method : other: standard NTP methodology

Year : 1986 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method: Methods are described in detail in Section 5.7

(Carcinogenicity).

Samples of the following tissues were subject to

histopathological evaluation:

Integumentary system
Respiratory system
Haematopoietic system
Circulatory system
Digestive system
Urinary system
Endocrine system
Reproductive system
Nervous system
Special sense organs
Musculoskeletal system

Body cavity Adipose tissue

Any tissue appearing abnormal at necropsy.

Result : Body weight and clinical signs

Treated animals showed a dose-related reduction in body weight. Final body weights were approx. 5% lower than control for low dose animals, and 14% and 24% lower then

control in the high dose male and female groups, respectively. No clinical signs are described.

Survival

The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.001) less than that of the low dose females and controls. Mortality and morbidity was especially marked at wk 94 of the study. Survival in males was comparable for all groups (78%, 84% and 82% alive at wk 103 for the control, 62 mg/kg bwt/d and 125 mg/kg bwt/d groups, respecti vely).

Non-tumor pathology

The incidence of heptic foci of clear change (22% versus 6% in controls) and liver necrosis (focal and centrilobular combined; 18% versus 2% in controls) were increased in high dose female rats only. The incidence of other lesions in the treated animals was similar or lower than that of the controls.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Under the conditions of the study, the chronic NOEL for PDC

in male rats was 62 mg/kg bw/d (based upon a reduction in final body weight observed at 125 mg/kg bw/d). The NOEL in females was 125 mg/kg bw/d (based upon lower body weight, lower survival and liver lesions present in the 250 mg/kg

bw/d group).

Reliability : (1) valid without restriction

Comparable to guideline study, with restrictions.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Sub-acute
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 14 days

Frequency of treatm. : Consecutive days

Post exposure period : One day

Doses : 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d

Control group : yes, concurrent vehicle

NOAEL : = 250 mg/kg bw

LOAEL : = 125 mg/kg bw

Method : other: standard NTP methodology

Year : 1986 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Groups of 5 male and 5 female B6C3F1 mice (age 6 wk at start

of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d for 14 consecutive days, followed by one day of

bw/d for 14 consecutive days, followed by one day of

observation. The animals were group housed (5/sex/cage) and

observed twice daily for mortality.

Necropsies were performed on all animals (macroscopic observations only, no histopathology included).

The concentration of test article in the dosing solutions

was verified using GC-FID.

Result : GC analysis of the dosing solutions demonstrated that the

achieved concentration was 95 - 100% of target.

All male mice receiving 1000 or 2000 mg/kg bw/d and 3/5 given 500 mg/kg bw/d died during the study. All females from the 2000 mg/kg bw/d group, and 4/5 from the 1000 mg/kg bw/d

group also died pre-study termination.

Final mean body weight for the surviving mice was unaffected by treatment.

The renal medullae were red in all mice of both sexes from the 2000 mg/kg bw/d group, the majority of males given 500 mg/kg and the majority of females given 1000 mg/kg bw/d. This change was also present in single females from all other dose groups.

No other compound-related effects were observed at necropsy.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, the sub-acute NOEL for

PDC in male mice was 250 mg/kg bw/d. No NOEL was established

for female mice (LOEL 125 mg/kg bw/d).

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type Sub-chronic Species mouse Sex male/female Strain B6C3F1 Route of admin. gavage Exposure period 13 wk Frequency of treatm. : 5 d/wk Post exposure period None

Doses : 0, 30, 60, 125, 250 or 500 mg/kg bw/d

Control group : yes, concurrent vehicle

NOAEL : = 500 mg/kg bw

LOAEL : >= 500 mg/kg bw

Method : other: standard NTP methodology

Year : 1986 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Groups of 10 male and 10 female B6C3F1 mice (age 9 -10 wk at

start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 30, 60, 125, 250 or 500 mg/kg bw/d 5 d/wk for 13 wk. The animals were group housed and observed daily for clinical signs and twice daily for mortality. Animals judged to be moribund were taken to necropsy. Each animal was given a detailed weekly examination, including palpation for tissue masses or

swelling. Body weights were taken weekly.

Necropsies were performed on all surviving animals at the end of the treatment period. A comprehensive range of tissues were sampled and preserved, and those from the controls and the 500 mg/kg groups subject to microscopic examination.

The concentration of test article in the dosing solutions was verified using GC-FID.

Result : GC analysis of the dosing solutions demonstrated that the

achieved concentration was 05 1000/ of target

achieved concentration was 95 - 100% of target.

One male given 60 mg/kg bw/d died during the first week of the study, and a female from the 500 mg/kg bw/d group died

during wk 12.

Body weights for all treated males were decreased 4-5% (ie no dose-relationship present). Body weights for females from the 250 mg/kg and 500 mg/kg groups were also decreased slightly by 3-4%. Since there were no histopathological changes noted, these minor effects on body weight are considered incidental and not related to treatment.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, the sub-chronic NOEL for

PDC in the mouse was 500 mg/kg bw/d.

Reliability : (1) valid without restriction

 $Comparable \ to \ guideline \ study.$

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 103 wk
Frequency of treatm. : 5 d/wk

Post exposure period

 Doses
 : 0, 125 or 250 mg/kg bw/d

 Control group
 : yes, concurrent vehicle

 NOAEL
 : <= 125 mg/kg bw</td>

 LOAEL
 : = 125 mg/kg bw

Method : other: standard NTP methodology

Year : 1986 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method: Methods are described in detail in Section 5.7

(Carcinogenicity).

Samples of the following tissues were subject to

histopathological evaluation:

Integumentary system
Respiratory system
Haematopoietic system
Circulatory system
Digestive system
Urinary system
Endocrine system
Reproductive system
Nervous system
Special sense organs
Musculoskeletal system

Body cavity Adipose tissue

Any tissue appearing abnormal at necropsy.

Result: Body weight and clinical signs

Mean body weights of treated and vehicle control animals

were comparable, and no compound-related clinical signs were

noted.

Survival

The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.035) less than that of the low dose

females and controls, with 70%, 58% and 52% of the control, low and high dose animals surviving to termination. Survival

in males was comparable for all groups (70%, 66% and 70% alive at wk 103 for the control, 125 mg/kg bwt/d and 250 mg/kg bwt/d groups, respectively). The report notes that the lowered survival in female mice was related to an increased incidence of reproductive tract infections in animals which died before the end of the study (45% of controls versus 64% of the low and high dose females that died during the study).

Non-tumor pathology

Hepatocytomegaly (6%, 10% and 30% for control, low dose and high dose animals, respectively) and hepatic focal necrosis (4%, 10% and 20%) were seen in male mice only.

Acanthosis of the surface epithelium of the forestomach occurred at increased incidence in high dose males (0%, 0%, 4%) and both groups of females (0%, 10%, 8%).

Suppurative inflammation (affecting ovary, uterus or multiple organs, and a presumed consequence of reproductive tract infection) was found in 5/11 control, 9/14 low dose and 14/22 high dose females that died before the end of the study.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Under the conditions of the study, the chronic LOAEL for PDC

in mice was 125 mg/kg bw/d (based upon liver lesions in male mice and a canthosis of the stomach in females). The NOAEL $\,$

was <125 mg/kg bwt/d.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Sub-chronic

Species : rat

Sex : male/female
Strain : Fischer 344
Route of admin. : inhalation
Exposure period : 13 wk
Frequency of treatm. : 6 hr/d, 5 d/wk

Post exposure period

Doses : 0, 15, 50 or 150 ppm (0, 0.068, 0.225 or 0.675 mg/l)

Control group : yes, concurrent vehicle

NOAEL : = 15 ppm

Method

 Year
 : 1988

 GLP
 : yes

Test substance : other TS: 99.4% purity

Method : Animals and treatments

Male and female F344 rats (n = 10 per group, age 7-8 wk at start of treatment) were exposed whole body to 0, 15, 50 or 150 ppm PDC vapor (0, 0.068, 0.225 or 0.675 mg/l) 6 hr/d, 5 d/wk for 13 wk. The test atmosphere was generated by passing heated air (50 degrees) though a J-tube containing a measured amount of PDC. The chamber volume was 4100 l (stainless steel and glass construction; 1 chamber per exposure group) and total airflow was 800 l/min (12 air changes/hr). The distribution of PDC within the chamber was determined 1-2 times/hr at 9 sampling points using a MIRAN

1A infrared spectrometer.

Observations

Animals were examined after each exposure period for clinical signs or indications of overt toxicity.

Haematology

Packed cell volume (PCV), red blood cell counts (RBC), haemoglobin (HGB), white blood cell counts (WBC), mean red cell volume (MCV), mean red cell haemoglobin (MCH), mean red cell haemoglobin concentration (MCHC), platelet counts (PLAT) and differential white cell counts were determined approx. 2 wk prior to study termination using blood collected by orbital sinus puncture.

Clinical chemistry

Total bilirubin (TBILI), serum glutamic pyruvic transaminase (SGOT), serum glutamic oxaloacetatic transaminase (SGPT), alkaline phosphatase (AP), urea nitrogen (UN) and glucose (GLUC) were determined on blood (cervical vein) collected at necropsy. Red blood cell and plasma cholinesterase were quantified on blood collected by orbital sinus bleed apporx. 2 wk prior to sacrifice.

Urine analysis

Specific gravity (refractive index; American Optical Co), pH, glucose, ketones, bilirubin, occult blood and protein (Chemstrip 7, Bio-Dynamics) were determined approx. 2 wk prior to sacrifice.

Necropsy

Rats were sacrificed on the day after the last exposure following an overnight fast. The eyes and internal organs were subject to macroscopic examination, and the weights of the brain, heart, liver, kidneys, thymus and testes recorded. Approx. 50 tissues were sampled, preserved and processed for microscopic examination (haematoxylin and eosin).

Statistical methods

Clinical chemistry, haematology, urine analysis and organ weights were analysed using Bartlett's test for equality of variances, followed by parametric or non-parametric ANOVA with Dunnet's test or the Wilcoxon Rank-Sum test with Bonferroni's correction for multiple comparisons. The final interpretation of the results considered whether an orderly exposure-response relationship was apparent in the data since a high occurrence of Type I (false positive) errors would be anticipated due to the large number of statistical comparisons that were included in this study.

IR analysis demonstrated that the mean concentration of PDC within the chamber (SD in brackets) was 0, 15(1), 50(3) or 151(3) ppm.

Clinical observations and body weight
One male rat from the 15 ppm group died on day 81 from
haemorrhagic cystitis; this was considered a spontaneous
event by the study pathologist. No other clinical or overt
signs of toxicity were recorded in any of the treated
animals during the 90 d exposure period.

Body weights for high dose animals were significantly decreased throughout the study (females decreased 7% at termination, males 10%), with a smaller (non-significant)

Result

decrease apparent in mid-dose animals from wk 2 onwards (4-8% decrease at termination).

Haematology and urine analysis

There were no toxicologically or statistically significant changes in haematological or urine parameters in any of the treatment groups.

Clinical chemistry

SGPT values from all treated females were decreased 25-31% relative to controls, while SGOT from females exposed to 15 or 50 ppm PDC were decreased 18-21% (no effect in high dose animals). Serum glucose was decreased 22% in mid dose males only. None of these changes were considered toxicologically significant by the study authors.

Necropsy findings

Several slight but statistically significant effects in organ weights were noted in rats exposed to 50 or 150 ppm PDC for 13 wk i.e. relative brain weight increased 8% and relative heart weight increased 6% in mid dose males, absolute brain weight decreased 3% in high dose females. A qualitative reduction in the amount of abdominal adipose tissue was also noted in some high dose males. These changes were considered of negligible toxicological relevance by the study authors (secondary to lower bwt).

Histopathology

Histopathological effects were confined to the upper respiratory tract. Very sight or slight degeneration of the olfactory mucosa in the anterior portion of the nasal cavity was noted for all rats exposed to 50 or 150 ppm PDC (no effect at 15 ppm). Very slight or slight hyperplasia of the respiratory mucosa was also present in the majority of rats (both sexes) exposed to 50 or 150 ppm PDC, with very slight hyperplasia detected in around one quarter of the low dose group. This hyperplasia was focally restricted to the anterior portion of the nasal tissues and considered by the study pathologist to be an adaptive, protective response. Chronic inflammation of nasal tissue was present in all groups, including controls, but was slightly more prevalent in high dose rats of both sexes.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Minimal toxicological effects were recorded in male and female F344 rats following whole body exposure to 0, 15, 50 or 150 ppm PDC for 13 wk. Treatment related effects were

or 150 ppm PDC for 13 wk. Treatment related effects were limited to a minor reduction in body weight (NOAEL = 15 ppm), and very slight hyplasia of the nasal respiratory epithelium considered to be an adaptive/protective response

by the study authors (NOAEL of 15 ppm).

Reliability : (1) valid without restriction

Comparable to guideline study.

: Critical study for SIDS endpoint

25.10.2004

Type : Sub-chronic Species : mouse

Sex

Flag

Strain : B6C3F1
Route of admin. : inhalation
Exposure period : 13 wk
Frequency of treatm. : 6 hr/d, 5 d/wk

Post exposure period

Doses : 0, 15, 50 or 150 ppm (0, 0.068, 0.225 or 0.675 mg/l)

Control group : yes, concurrent vehicle

NOAEL : = 150 ppm

Method

Year : 1988 **GLP** : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female B6C3F1 mice (n = 10 per group, age 7-8 wk at start of treatment) were exposed whole body to 0, 15, 50 or 150 ppm PDC vapor (0, 0.068, 0.225 or 0.675 mg/l) 6 hr/d, 5

d/wk for 13 wk.

See previous record for details of test atmosphere generation, in-life observations, haematology (orbital sinus puncture at termination).

Necropsy

Mice were sacrificed on the day following the last exposure

(no overnight fast). See previous record for further

details.

Statistical methods See previous record.

Result : IR analysis demonstrated that the mean concentration of PDC

within the chamber (SD in brackets) was 0, 15(1), 50(3) or

151(3) ppm.

Clinical observations and body weight

No clinical signs or evidence of overt toxicity were recorded in any of the treated animals, while body weights

were indistinguishable from those of the controls.

Haematology

RBC and HGB were slightly but significantly decreased (approx. 5%) in low and high dose male mice (no effect at 50 ppm, all treated females indistinguishable from controls). PCV was statistically significantly increased in low dose animals (no effect in mid and high dose groups). The authors concluded these findings were of doubtful toxicological relevance given the lack of a clear dose-response

relationship and an absence of histopathological involvement

in bone marrow or spleen. All other heamatological

parameters were comparable between the control and treated

animals.

Necropsy findings

Body weight and organ weights (relative and absolute) were

unaffected by treatment.

Histopathology

No treatment related histopathological changes were present.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : No adverse treatment related changes were noted in male and

female B6C3F1 mice following whole body exposure to to 0, 15, 50 or 150 ppm PDC for 13 wk (NOAEL = 150 ppm).

: (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

Reliability

25.10.2004 (187)

Type : Sub-chronic
Species : rabbit
Sex : male/female
Strain : New Zealand white

Route of admin. : inhalation
Exposure period : 13 wk
Frequency of treatm. : 6 hr/d, 5 d/wk

Post exposure period

Doses : 0, 150, 500 or 1000 ppm (0, 0.675, 2.25 or 4.5 mg/l)

Control group : yes, concurrent vehicle

LOAEL : = 150 ppm

Method

Year : 1988 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female NZW (n = 7 per group, age approx. 7 mo at start of treatment) were exposed whole body to 0, 150, 500 or 1000 ppm PDC vapor (0, 0.675, 2.25 or 4.5 mg/l) 6 hr/d, 5

d/wk for 13 wk.

See previous record for details of test atmosphere

generation

Observations

Animals were examined after each exposure period for clinical signs or indications of overt toxicity.

Haematology

Haematological assessments (see previous record) were conducted on blood collected by venipuncture 2 wk prior to study termination. Additional blood samples were collected at necropsy and the analyses extended to include nucleated red blood cells and reticulocyte count.

Clinical chemistry

See previous record for details of parameters assessed.

Necropsy

Rabbits were sacrificed on the day following the last exposure (no overnight fast). See previous record for

further details.

Statistical methods See previous record.

Result : IR analysis demonstrated that the mean concentration of PDC

within the chamber (SD in brackets) was 0, 151(3), 502(7) or

1003(8) ppm.

Clinical observations and body weight

No clinical signs or evidence of overt toxicity were recorded in any of the treated animals, while body weights

were indistinguishable from those of the controls.

Haematology

Analysis of blood samples collected 2 wk prior to study termination showed that RBC were significantly decreased in rabbits exposed to 150 ppm (10% decrease, males only), 500 ppm (both sexes, approx. 15-20%) or 1000 ppm (both sexes, approx. 20-25%) PDC vapor. HGB was decreased (both sexes) in

ld 78-87-5 5. Toxicity Date 14.12.2004

> mid (10-13%) and high (14-16%) dose rabbits. PCV was decreased (both sexes) in mid (11-15%) and high (17%) dose rabbits. MCV and MCH increased (both sexes) in a non-significant but apparently dose-related manner.

Essentially similar changes in RBC, HGB and PCV were present in blood samples collected at study termination. In addition, the number of nucleated erythrocytes was non-significantly increased in males exposed to 1000 ppm PDC, while the percentage of reticulocytes (regenerative response) was increased significantly in mid (approx. 2-fold) and high (3-4 fold) dose animals of both sexes. MCV and MCH were again increased in all treated animals.

Overall, these findings were consistent with regenerative macrocytic normochromic anemia.

Clinical chemistry

No treatment related changes were recorded.

Necropsy findings

Absolute liver weights from mid and high dose males were significantly increased by approx. 25-30%, and relative liver weight significantly increased by approx. 20%. Supplemental information presented in the study report demonstrates that absolute liver weights values from treated animals (107.9 - 122.0 g) were within the historical range for control male rabbits from the laboratory conducting this study (93.8 - 130.3 g), while the controls (93.8 g) were at the lower limit of the historical data. The authors conclude that these liver weight changes were not indicative of a treatment related effect. No other organ weight changes or gross lesions were present.

Histopathology

Bone marrow hyperplasia (regenerative response) was present in some rabbits exposed to 500 or 1000 ppm PDC vapor (NOAEL = 150 ppm), with a qualitative increase in haemosiderin-laden macrophages noted in bone marrow from high dose animals. Minimal degeneration of olfactory epithelium occurred in nasal tissue from all groups, including the controls, however the prevalence in high dose males (5/7 affected, versus 2/7 controls) was considered suggestive of a treatment-related effect by the study authors (NOAEL = 500 ppm). No other treatment related histopathological changes were observed.

Source Conclusion The 1,2-Dichloropropane ICCA/HPV Consortium

Minimal toxicological effects were recorded in male and female NZW rabbits following whole body exposure to 0, 150, 500 or 1000 ppm PDC for 13 wk. Treatment related, toxicologically significant changes were limited to alterations in red cell parameters (decreased RBC, HGB, PCV) in male rabbits exposed to 150-1000 PDC for 13 wk (LOAEL = 150 ppm), and in females exposed to 500 or 1000 ppm over the same period of time (NOAEL = 150 ppm). The overall pattern of changes was consistent with a regenerative macrocytic normochromic anemia. Minimal degeneration of olfactory epithelium in high dose males (NOAEL = 500 ppm; females unaffected) was also observed.

Reliability

(1) valid without restriction Comparable to guideline study.

Hag : Critical study for SIDS endpoint

25.10.2004 (187)

Type : Sub-acute Species : rat

Sex: male/femaleStrain: Fischer 344Route of admin.: gavageExposure period: 14 days

Frequency of treatm. : Consecutive days

Post exposure period : One day

Doses : 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d

Control group: yes, concurrent vehicleNOAEL: = 500 mg/kg bwLOAEL: = 1000 mg/kg bw

Method : other: standard NTP methodology

Year : 1986 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Groups of 5 male and 5 female F344 rats (age 6 wk at start

of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 125, 250, 500, 1000 or 2000 mg/kg

bw/d for 14 consecutive days, followed by one day of

observation. The animals were group housed (5/sex/cage) and

observed twice daily for mortality.

Necropsies were performed on all animals (macroscopic

observations only, no histopathology).

The concentration of test article in the dosing solutions

was verified using GC-FID.

Result : GC analysis of the dosing solutions demonstrated that the

achieved concentration was 95 - 100% of target.

All rats given 2000 mg/kg bw died during the study, along with a single male from the 125 mg/kg bw/d group.

Final mean body weight was decreased 14-15% in animals given

1000 mg/kg bw/d relative to the controls.

The renal medullae were red in 4/5 males and 5/5 females given 2000 mg/kg bw/d but not in rats from the lower

treatment groups.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : Under the conditions of the study, the sub-acute NOEL for

PDC in male and female rats was 500 mg/kg bw/d.

Reliability : (1) valid without restriction

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type :
Species : rat
Sex : no data
Strain : no data
Route of admin. : inhalation
Exposure period : 2 - 5 days
Frequency of treatm. : 7 hours/day

Post exposure period :

Doses : 10400 mg/m3
Control group : no data specified

Method : other: Repeated Dose Toxicity

ld 78-87-5 5. Toxicity Date 14.12.2004

Year 1946 GLP no data Test substance no data

Remark Mortality: 5/20

> The histopathologic evaluation of 3 surviving animals showed visceral congestion, centrilobular fatty degeneration in the liver with atrophic and necrotic changes, hemosiderosis in the spleen and myelosis and bronchitis with pneumonia. In addition, lipoid atrophy was found in the adrenal cortex; 20

animals/exposure group.

The 1,2-Dichloropropane ICCA/HPV Consortium Source

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type **Species** rat Sex male

Strain Sprague-Dawley

Route of admin. gavage **Exposure** period 5 and 10 days daily

Frequency of treatm. Post exposure period

Doses 100, 250, 500 and 1000 mg/kg body weight/day

Control group yes, concurrent vehicle LOAEL = 100 mg/kg bw

Method other: Repeated Dose Toxicity

Year 1989 : GLP : no data

Test substance other TS: purity = 99 %

Remark Depending on dosage, animal body weight was reduced (no

> specific information) and sedation was detected. The highest dose was given for 5 days resulting in a significant (p <= 0.05) increase of sorbitol dehydrogenase transferase reactivity and alanine aminotransferase reactivity as well as urea content in the blood. After 10 days, only increase of urea content persisted. Doses given above 100 mg/kg, after days 5 and 10, the content of microsomal cytochrom P-450 in the liver decreased significantly (p \leq 0.05). After 5 days using >= 250 mg/kg, the non-proteinsulfhydryl-content in the liver was significantly (p <= 0.05) decreased (dose-related). After 10 days of dosing, only the group with highest dose adminstered showed a significant (p <= 0.05) reduction in NPSH. After days 5 and 10 using >= 250mg/kg, the non-protein-sulfhydryl-content in the kidney was significantly (p <= 0.05) increased. After 5

davs of

treatment, histopathological changes were found only in the liver. Jaundice was diagnosed, characterized by necrosis of

the centrilobular hepatocytes, inflammatory cell infiltration and proliferation of fibroblasts. The changes appeared in all animals treated with 1000 mg/kg. In the group tested with 250 and 500 mg/kg, less than 50% of the animals showed changes (no further information). 5 days later symptoms persisted only in the two groups receiving highest doses but in a less intensive form. After days 5 and 10 of dosing, a hemolytic anemia was diagnosed in the

kidney; 6 - 8 animals/dosage and control group.

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (188)

Type : Species : rat Sex : male

Strain : Sprague-Dawley

Route of admin. : gavage
Exposure period : 13 weeks
Frequency of treatm. : 5 days/week

Post exposure period

Doses : 100, 250, 500 and 750 mg/kg body weight/day

Control group : yes, concurrent vehicle
LOAEL : = 100 mg/kg bw

Method : other: Repeated Dose Toxicity

Year : 1989 GLP : no data

Test substance : other TS: purity = 99 %

Remark: The body weight gain was decreased significantly (p <= 0.05)

at concentrations >= 100 mg/kg (dose related). All animals of the 750 mg/kg dosage group died or were killed moribund

after the first 2 weeks of treatment. Mortality in the 500

mg/kg dosage group was approximately 60 %. In the 750 mg/kg

dosage group the following histopathological changes appeared: light hepatitis, hemosiderosis in the spleen, vacuolization of medulla, lipidosis of the renal cortex, reduced sperm count and appearance of degenerated

spermatogonia in the epididymis. Doses of

1,2-dichloropropane induce hemolytic anemia. Animals treated with 250 and 500 mg/kg, showed significantly (p <= 0.05)

decreased hemoglobin and hematocrit in serum;

histopathologic examination showed hemosiderosis and hyperplasia of the erythropoietic elements in the spleen for

most animals in all dosage groups.

Only animals from the 500 mg/kg dosage group showed

histopathologic changes in the liver (periportal

vacuolization and fibroplasia). Relative weight of liver and spleen in dosage groups 250 and 500 mg/kg and relative weight of kidney in dosage group 500 mg/kg were

significantly (p <= 0.05) increased; 15 - 16 animals/dosage

and control group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (188)

Type : Species : rat

Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13 weeks
Frequency of treatm. : 5 days/week

Post exposure period

Doses : 60, 125, 250, 500 and 1000 mg/kg body weight/day

Control group : yes, concurrent vehicle

NOAEL : = 250 mg/kg bw

LOAEL : = 500 mg/kg bw

Method : other: Repeated Dose Toxicity

Year : 1986 GLP : no data

Test substance : other TS: purity = 99.4 %

Remark: All animals in the highest dosage group died as well as 5

male animals of the 500 mg/kg dosage group. Compared to the control group, the body weight of the male animals in the 500 mg/kg dosage group was reduced by 16 % at test conclusion. Histopathologic changes in the form of fatty degenerations and centril obular necrosis appeared in the liver in 2 of 10 female rats, centrilobular congestion was found in 5 of 10 male rats and in 2 of 10 female rats of the 1000 mg/kg dosage group; 10 animals/sex/dosage and control

group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (186)

Type : Species : rat

Sex: male/femaleStrain: Fischer 344Route of admin.: gavageExposure period: 13 weeksFrequency of treatm.: 5 days/week

Post exposure period

Doses : 20, 65 and 200 mg/kg body weight/day

Control group : yes, concurrent vehicle

Method : other: Repeated Dose Toxicity

Year : 1988 **GLP** : yes

Test substance : as prescribed by 1.1 - 1.4

Remark: On the first 2 - 3 days of treatment, the animals showed

increase of lacrimation and blink (dose related), as well as decreased spontaneous locomotion. Body temperature of the 200 mg/kg dosage group compared to the control group was significantly (p <= 0.05) reduced after the treatment period (females 0.6 degrees C, males 0.3 degrees C). The neurological and neurohistopathological tests showed no

substance related changes.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (189)

Type : Species : rat

Sex: male/femaleStrain: Fischer 344Route of admin.: gavageExposure period: 103 weeksFrequency of treatm.: 5 days/week

Post exposure period : no

Doses : male animals: 62 or 125 mg/kg body weight/day; female animals: 125 or

250 mg/kg body weight/day

Control group : yes, concurrent vehicle

NOAEL : =

LOAEL : =

Method : other: Carcinogenicity Study

Year : 1979 **GLP** : no data

Test substance : other TS: purity = 99.4 %

Remark: 50 animals/sex/dosage and control group

Result : Body weight gain was decreased (dose related) in male and

female animals. Mortality for females was increased significantly (p < 0.001) in the 250 mg/kg dosage group (26 % control, 14 % 125 mg/kg, 68 % 250 mg/kg). For females in the high dosage group an increased incidence of focal and

centrilobular liver necrosis (2/50, 1/50 or 12/50), foam cell foci (3/50, 5/50 or 11/50) and a light

hemosiderosis in the spleen was observed. All other tumors relating to type, incidence and time of formation were equal to the control group. No substance related, histopathologic, non-neoplastic changes appeared other than the ones mentioned above. Female animals were diagnosed more often with mammary carcinoma (dose related) (1/50, 2/50 and

with mammary carcinoma (dose related) (1/50, 2/50 and 5/50; historic control of the research institute: 3/50).

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (186)

 Type
 :

 Species
 :
 rat

 Sex
 :
 male

 Strain
 :
 Wistar

 Route of admin.
 :
 i.p.

 Exposure period
 :
 4 weeks

 Frequency of treatm.
 :
 5 days/week

Post exposure period

Doses : 10, 25, 50, 100, 250 and 500 mg/kg body weight/day

Control group : yes, concurrent vehicle
LOAEL : <= 10 mg/kg bw

Method : other: Repeated Dose Toxicity

Year : 1988 GLP : no data

Test substance : other TS: purity = 97 %

Remark: One animal from the 500 mg/kg group died after injection

number 15. After a 5-day treatment of 500 mg/kg, activity of glutathione-S-transferase in the liver was significantly (p < 0.025) increased and the activity of the angiotensin converting enzyme in the striated border of the

proximal kidney tubuli was significantly (p < 0.025)

decreased. After a 4-week treatment the following biological changes in the liver were observed: content of reduced

glutahione (GSH) as well as the activity of

glutahione-S-transferase >= 50 mg/kg significantly (p < 0.025) increased; cytochrome P-450 activity >= 250 mg/kg and the activity of aminopyridindesmethylase >= 100 mg/kg significantly (p < 0.025 and p < 0.05) decreased. In the renal cortex, the GSH content >= 250 mg/kg and activity of glutathione-S-transferase in the 500 mg/kg dosage group was significantly (p < 0.05) increased. The cytochrome P-450 activity was significantly (p < 0.05) decreased in the

highest dosage group; the angiotensin converting enzyme activity in the striated border of the proximal renal tubuli

was significantly (p < 0.025) decreased >= 100 mg/kg (dose related). The histopathological analysis during the dissection indicated specifically regenerative, hyperplastic changes >= 10 mg/kg after a 4-week treatment. In the kidney, the 4-week treatment of 1,2-dichloropropane resulted in a necrosis of striated border in the highest dosage groups as well as mesangial glomerular nephritis (dose related) with mesangial and sub-epithelial granular sedimentation >= 50 mg/kg; 5-10 animals per dosage and

control group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (190) (178) (191)

Type

Species: mouseSex: male/femaleStrain: B6C3F1Route of admin.: gavageExposure period: 13 weeksFrequency of treatm.: 5 days/week

Post exposure period

Doses : 30, 60, 125, 250 and 500 mg/kg body weight/day

Control group : yes, concurrent vehicle
NOAEL : >= 500 mg/kg bw

Method : other: Repeated Dose Toxicity

Year : 1986 GLP : no data

Test substance : other TS: purity = 99.4 %

Remark: No changes were found in the reduction of body weight,

mortality or histopathologic changes using

1,2-dichloropropane; 10 animals/sex/dosage and control

group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (186)

Type :

Species: mouseSex: male/femaleStrain: B6C3F1Route of admin.: gavageExposure period: 103 weeksFrequency of treatm.: 5 days/week

Post exposure period : no

Doses: 125 or 250 mg/kg body weight/day

Control group : yes, concurrent vehicle

NOAEL : = LOAEL : =

Method : other: Carcinogenicity Study

Year : 1979 GLP : no data

Test substance : other TS: purity = 99.4%

Remark: 50 animals/sex/dosage and control group

Result : Mortality increased s ignificantly (p < 0.05) in female

animals in the 250 mg/kg dosage group (48% compared to 30%

in the control group). The number of liver adenomas increased in male animals (7/50 in the control group, 10/50 in the 125 mg/kg dosage group, 17/50 in the 250 mg/kg dosage group; and the incidence of liver adenomas and carcinomas increased in females and in males (females: 2/50, 8/50, p < 0.05, 9/50, p < 0.05; males: 18/50, 26/50, 33/50, p < 0.01). Papillomas with keratinization appeared in the pre-stomach: male animals 1/48 (125 mg/kg), 3/49 (250 mg/kg), female

animals 2/50 (125 mg/kg), 2/50 (250 mg/kg). In the control group, these findings did not appear.

The male animals treated with substance suffered more often with hepatocytomegaly (3/50, 5/49 and 15/50) and liver necrosis (2/50, 5/49, 10/50 control group, 125 and 250 mg/kg). Two female animals in the 250 mg/kg dosage group were diagosed with follicular carcinoma and 3 female animals

were

diagnosed with follicular adenoma of the thyroid gland.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (186)

Type :

Species: rabbitSex: no dataStrain: no dataRoute of admin.: inhalationExposure period: 2 - 5 daysFrequency of treatm.: 7 hours/day

Post exposure period :

Doses : 10400 mg/m3
Control group : no data specified

Method : other: Repeated Dose Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark : Mortality: 2/3.

The histopathologic evaluation of 3 surviving animals showed visceral congestion, centrilobular fatty degeneration in the liver with atrophic and necrotic changes, hemosiderosis in spleen and myelosis and bronchitis with focal pne umonia; 3

animals/exposure group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type :

Species : rabbit Sex : female

Strain : New Zealand white

Route of admin. : gavage
Exposure period : 13 days
Frequency of treatm. : daily
Post exposure period : no

Doses: 250, 500 and 1000 mg/kg body weight/day

Control group : yes, concurrent vehicle

LOAEL : <= 250 mg/kg bw

Method : other: Repeated Dose Toxicity

Year : 1988 **GLP** : yes

Test substance : as prescribed by 1.1 - 1.4

Remark: All rabbits in the two high dose groups and one rabbit in

the 250 mg/kg-dose group died or were killed moribund during the test period. The animals of the high dose group, before dying, showed lethargy and ataxy. All treated animals showed a decreased gain of body weight. Necrosis of the liver was detected in all dead animals per above, given 500 and 1000 mg/kg. Some of these animals suffered light anemia and dilation of renal tubuli was prevelant; two animals/dosage

and control group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (192)

Type : dog
Species : dog
Sex : no data
Strain : no data
Route of admin. : inhalation

Exposure period : up to 128 exposures **Frequency of treatm.** : 7 hours/day, 5 days/week

Post exposure period : no

Doses : 4400 mg/m3 Control group : no data specified

Method : other: Repeated Dose Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark : Mortality: 4/9.

During dosing period, 3 dogs died between exposure 27 and 28 and 1 dog died after exposure 96. Fatty degeneration of the liver and the convoluted renal tubuli was detected in all animals that died. In addition, one dog was diagnosed with centrilobular congestion including atrophy and necrosis in the liver cells and 2 dogs were diagnosed with fatty degeneration of the heart and lipoid atrophy in the renal cortex. One dog dying after 28 exposures was observed with congestion, atrophy and focal necrosis in zona reticularis of the adrenal gland. Some of the surviving 5 dogs were killed after 55 single exposures and the rest after 128 exposures. These 5 dogs showed no histopathological differences compared with the control group; 9 dogs/exposure

: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Туре

Source

Species: guinea pigSex: no dataStrain: no dataRoute of admin.: inhalationExposure period: 5 daysFrequency of treatm.: 7 hours/day

Post exposure period

Doses : 10400 mg/m3
Control group : no data specified

Method : other: Repeated Dose Toxicity

Year : 1946
GLP : no data
Test substance : no data

Remark: Whole-body exposure; mortality 11/16. Fatty degeneration

of the liver was detected during the dissection.

Multilobular and centrilobular congestion with atrophy and necrosis of liver cells was detected in 3 animals. Necrotic liver foci with infiltrated neutophils was diagnosed in 1 animal. An increased build up of a fatty degeneration in the kidneys and necrosis in the adrenal glands was observed. In addition the animals were suffering with hemosiderosis in the spleen and congestion in the lung; 16 animals/exposure

group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (174)

Type :

Species : other: rat, guinea pig and dog

Sex : male/female
Strain : no data
Route of admin. : inhalation
Exposure period : 128 to 140 hours

Frequency of treatm. : 7 hours/day, 5 days/week

Post exposure period no data : **Doses** 400 ppm : **Control group** : yes NOAEL : = LOAEL : Method other : 1948 Year **GLP** no **Test substance** no data

Result : Rats, guinea pigs and dogs received from 128 to 140

seven-hour inhalation exposures. No ill effects were observed that could be attributed to the exposures except for decreased weight gain in the rats. Histological examination showed no changes specifically attributable to

1,2-dichloropropane.

There was a heavy mortaltiy rate among mice exposed to 400 ppm of 1,2-dichloropropane. Hepatomas was found in 3 animals of the susceptible C3H strain, which were histologically

similar to mice repeatedly exposed to carbon tetrachloride.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (193)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Bacterial reverse mutation assay

System of testing : Salmonella typhimurium TA98, TA1537, TA100 and TA1535

Test concentration : 0 (DMSO), 33, 100, 333, 1000 and 2000 ug/plate

Cycotoxic concentr. : > 2000 ug/plate

Metabolic activation : with and without

Result : negative

Method : other: liquid preincubation method

Year : 1986 GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : PDC was dissolved in DMSO and incubated with the tester

strains in suspension culture for 20 min prior to the addition of soft agar and plating-out. Exogenous metabolic activation was provided by liver S-9 preparations from Arochlor-1254 induced rats and hamsters. Each concentration

was tested in triplicate, and the entire study run twice.

Result: There was no increase in number of revertants in any of the

tester strains either in the absence or presence of rat or

hamster S-9 fraction.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: PDC was not mutagenic to Salmonella typhimurium TA98,

TA1537, TA100 or TA1535 in the presence or absence of S-9.

Reliability : (2) valid with restrictions

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Ames test

System of testing : Salmonella typhimurium TA98, TA1537, TA100 and TA1535

Test concentration : 0 (DMSO), 31.5, 100, 315, 1000 and 3150 nl/plate

Cycotoxic concentr. : >3150 nl/plate

Metabolic activation : with and without

Result : negative

Method : other: Ames et al. (1975) Mut Res 31, 347 - 364.

Year : 1979
GLP : no
Test substance : no data

Method : PDC (aqueous, 31.5 - 3150 nl/plate) was tested using a plate

incorporation method in two series of experiments in the presence or absence of S9 from Arochlor 1254-treated rats. There were two plates per concentration. Benzo(a)pyrene and MNNG were used as positive control substances in the absence of S9, and b enzo(a)pyrene, 2-aminoanthracene and 3MC as

positive controls in the presence of S9.

In a third series of tests, mutagenicity of PDC (3.15 - 3150 nl/plate; +S9) was evaluated in the presence of glutathione

supplementation (8 mg/plate).

Result: A satisfactory response was obtained with the positive

control substances.

No mutagenic repsonse was obtained with PDC, both in the absence or presence of S9. Glutathione supplementation was

without effect.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : PDC was not mutagenic to Salmonella typhimurium TA 98, TA

1537, TA 100 or TA 1535 when tested using a plate incorporation method in the presence or absence of S9.

Reliability : (2) valid with restrictions

Study well documented, meets generally accepted scientific

principles, acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (194)

Type : Ames test

System of testing : Salmonella typhimurium TA98, TA1537, TA100 and TA1535

Test concentration : vapour exposure: 0.3 - 10 ml PDC placed in a 20 l dessicator and

incubated with poured plates for 4 hr.

Cycotoxic concentr. : greater than maximum tested

Metabolic activation : with and without

Result : negative

Method : other: Ames et al. (1975) Mut Res 31, 347 - 364.

Year :

GLP : no Test substance : no data

Method : Poured plates, containing tester strain, cofactors and with

or without S9 fraction from Arochlor 1254-induced rats, were placed in a 20 l dessicator along with 0.3 - 10 ml PDC. Dichloroethane (3 ml) was used as positive control in the

presence and absence of S9.

A third series of plates were supplemented with 8 mg

glutathione.

After 4 hr incubation at 37 degrees C the plates were removed from the dessicator and incubated for a further 3

days in the dark.

Result: Dichloroethane was not mutagenic in the absence of S9 mix,

but a clear positive response was obtained in TA 100 and TA

1535 in the presence of S9.

No mutagenic repsonse was obtained with PDC, both in the

absence or presence of S9.

Glutathione supplementation was without effect.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : PDC vapour was not mutagenic to Salmonella typhimurium TA

98, TA 1537, TA 100 or TA 1535 when tested in a closed

system in the presence or absence of S9.

Reliability : (2) valid with restrictions

Study well documented, meets generally accepted scientific

principles, acceptable for assessment.

Flag : Critical study for SIDS endpoint

25.10.2004 (194)

Type : Ames test

System of testing : Salmonella typhimurium TA98, TA1537, TA100 and TA1535

Test concentration: 10-10000 ug/plate; 100-1500 ug/plate

Cycotoxic concentr. :

Metabolic activation: with and withoutResult: ambiguous

Method

Year : 1983 GLP : no data

Test substance : as prescribed by 1.1 - 1.4

Method : The mutagenic potential of 1,2-dichloropropane was

investigated in two laboratories (Case Warren Western Reserve, CWR; EG&G Mason, EGG) using a preincubation protocol. Hepatic S-9 was prepared from male SD rats (RL) and male Syrian hamster after induction with Arochlor 1254.

The report notes that results were interpreted in an ad hoc manner by each testing laboratory and by NTP personnel. The publication describes that a positive result was indicated by a "reproducible, dose-related increase, whether it be two-fold over background or not. "Statistical analysis was applied subsequently to data considered positive.

2-Aminoanthracene (all strains, plus rat and hamster S9), 4-nitro-o-phenylenediamine (TA98, -S9), sodium azide (TA100 and TA1535, -S9) and 9-aminoacridine (TA1537, -S9) were used as positive control.

: Although the number of revertants was increased in TA1535 and TA100 in the absence of S9, it is clear that the magnitude of this effect was always less than two-fold background.

Maximal increase in TA1535 over control: 56% at 1000 ug/plate (lab CWR) 75% at 3333 ug/plate (lab EEG)

Maximal increase in TA100 over control: 44% at 3333 ug/plate (lab CWR) 80% at 1500 ug/plate (lab EEG)

The results were incorrectly presented in the publications summary table as positive. The data in the appendix does not demonstrate a mutagenic response (less than a 2-fold increase). The data were reviewed by the Swiss CA and the UK CA at SIAM 17 and were determined to be negative.

No mutagenic activity was reported by either laboratory in TA98 or TA1537 at dose levels up to 3,333 ug/plate in the presence or absence of either source of S9.

PDC was without effect on the number of revertants recorded by either laboratory when tested using TA98 or TA100 in the presence of rat or hamster S9.

In the absence of S9, an apparent weak dose-response relationship was observed in TA1535:

In the absence of S9, an apparent weak dose-response relationship was observed in TA100:

CWR EGG		
0 (DMSO)	172	123
100	107	
333	141	
750	154	

Remark

Result

Id 78-87-5 5. Toxicity Date 14.12.2004

> 1,000 197 161 1,500 222 1,667 219 3,333 247 6.667 221 10.000 232

Source The 1,2-Dichloropropane ICCA/HPV Consortium Test substance Described as 'practical grade', purity not specified.

Reliability (2) valid with restrictions

25.10.2004 (195)

Ames test Type

System of testing Test concentration Cycotoxic concentr. Metabolic activation Result Method Year

GLP

as prescribed by 1.1 - 1.4 Test substance

Remark IARC summarises results obtained for 12 studies in

Salmonella typhimurium tester stains, with or without

exogenous activation.

Positive results were obtained with tester strains TA100 and

TA1535 both in the absence or presence of S9.

Negative results were obtained for tester strains TA100, TA1535 TA1537, TA1538 and TA1978 both in the absence and presence

of S9.

Negative results were obtained with TA1535 in the absence of

Overall, 4 out of 13 results were positive results in the absence of S9, and

4 out of 13 (31%) were positive in the presence of S9.

This information is presented in more detail in Attachment

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document Attachment 5.5.doc (2) valid with restrictions Reliability

Data from handbook or collection of data.

Flag Critical study for SIDS endpoint

25.10.2004 (196)

Type Mouse lymphoma assay

System of testing L5178Y

Test concentration 62.5-1000 nl/ml; 62.5-1000 nl/ml; 100-1000 nl/ml; Cycotoxic concentr. >800 nl/ml (above limit of solubility in test media)

Metabolic activation without Result negative Method

other: TK+/- Test

Year 1988 GLP no data : no data Test substance

Remark : 1,2-Dichloropropane was not very toxic in the absence of rat

S9 (except when the solubility limit was visibly exceeded ie 1000 nl/ml) and was evaluated by the authors as nonmutagenic

to L5178Y cells.

The authors comment that three trials were performed because weak mutagenic activity was suggested by a 1.5-fold increase in MF for the highest soluble dose of 750 nl/ml in the second trial. The third trial, however, yielded no response for doses up to 800 nl/ml and confirmed the lack of response

obtained in trial 1.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Study well documented, meets generally accepted scientific

principles, acceptable for assessment.

25.10.2004 (197)

Type : Mouse lymphoma assay

System of testing : L5178Y

Test concentration : 3.13-100 nl/ml; 10-80 nl/ml

Cycotoxic concentr.: 80 nl/mlMetabolic activation: withResult: positive

Method : other: TK+/- Test

Year : 1988
GLP : no data
Test substance : no data

Remark: The mutagenic potential of PDC in the presence of male rat

Arochlor 1254-induced S9 was investigated in two trials using concentration ranges of 0-100 nl/ml in the first and 0-80

nl/ml in the second.

When discussing these results, the authors comment that the first trial did not include a toxic treatment suitable for analysis, but that the highest assayed dose of 50 nl/ml (65% relative total growth; RTG) induced a 2.3-fold increase in mutation frequency. The mutant colony count was clearly elevated. The next highest dose of 100 nl/ml was lethal.

A different batch of S9, which appeared to be more active, was used in the second trial. A dose-related increase in MF was obtained over the 10-80 nl/ml dose range, with 80 nl/ml being highly toxic (6% RTG) and causing a 10-fold increase in MF.

They concluded that S9 activation was clearly therefore essential to the mutagenic activity of 1,2-dichloropropane. The increase in mutant frequency was due primarily to the

induction of small colony mutants.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Study well documented, meets generally accepted scientific

principles, acceptable for assessment.

25.10.2004 (197)

Type : Chromosomal aberration test

System of testing : CHO cells

Test concentration : -S9: 0 (DMSO), 1180, 1370 and 1580 ug/ml; +S9: 0 (DMSO), 460, 660 and

950 ug/ml

Cvcotoxic concentr. :

Metabolic activation : with and without

Result : positive

Method : other: standard NTP study design

Year : 1986

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method: In the absence of S9 CHO cells were incubated with serial

dilutions of PDC (up to 1580 ug/ml) or vehicle (DMSO) for 8-10 hr at 37 degrees C. Cells were then washed, and fresh medium containing colcemid (0.1 ug/ml) added. After a further 2-3 hr of incubation, cells were harvested and stained with Giemsa, and 100 cells per dose scored 'blind'

for chromosomal aberrations.

For tests in the presence of metabolic activation, cells were incubated with PDC (up to 950 ug/ml or vehicle) and rat S9 (Arochlor 1254-induced) for 2hr. Cells were then washed and incubated with fresh medium for a further 8-10 hr prior to processing as described above.

It is unclear if there was any independent repeat of the test.

Mitomycin C (0.125 ug/ml, no S9) and cyclophosphamide (50 ug/ml, plus S9) were used a positive controls.

No statistical analysis was applied to the results.

: Results are summarised in Attachment 5.5b.

The number of chromosomal aberrations/cell was increased 5 or >16 fold after incubation with 1370 or 1580 ug PDC/ml in the absence of S9. No clastogenic response was detected at 1180 ug/ml.

In the presence of S9, the number of aberrations/cell was increased 4 or >4 fold after incubation with 660 or 950 ug PDC/ml. No clastogenic effect was detected at 460 ug/ml.

A satisfactory response was obtained with the positive control substances.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 5.5b.doc

Conclusion : Under the conditions of the test, PDC increased the

occurence of chromosomal aberrations in CHO cells both in

the absence and in the presence of rat S9.

Reliability : (2) valid with restrictions

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Sister chromatid exchange assay

System of testing : CHO cells

Test concentration : 0 (DMSO), 112.7, 376.0 and 1127.0 ug/ml

Cycotoxic concentr.

Result

Metabolic activation : with and without

Result : positive

Method : other: standard NTP study design

Year

GLP : yes

Test substance: as prescribed by 1.1 - 1.4

Method : In the absence of S9 CHO cells were incubated with serial

dilutions of PDC (up to 1127.0 ug/ml) or vehicle (DMSO) for 2hr at 37 degrees C, followed by addition of BrdU (10 uM) and incubation for a further 24 hr. Cells were then washed,

fresh medium containing BrdU and colcemide (0.1 ug/ml) added and the incubation continued for another 2-3 hr. Samples were then fixed, stained with Giemsa, and fifty cells per dose from the top three dose levels (i.e. 112.7, 376.0 or 1127.0 ug PDC/ml) evaluated for SCEs. No further scoring was carried out if these results were clearly negative or positive. Scoring was carried out 'blind'.

For tests in the presence of metabolic activation, rat S9 (Arochlor 1254-induced) was added during the inital 2hr incubation with PDC or vehicle. Cells were then processed as described above.

Additional tests were performed to determine if PDC caused cell cycle delay, however no results are reported.

It is unclear if there was any independent repeat of the test

Mitomycin C (0.01 ug/ml, no S9) and cyclophosphamide (1.5 ug/ml, plus S9) were used a positive controls.

No statistical analysis was applied to the results. Results are summarised in Attachment 5.5a.

The number of SCE/cell was increased 2 or 3.5 fold after incubation with 376 or 1127 ug PDC/ml in the absence of S9.

In the presence of S9, SCE/cell were increased 2 or 2.5 fold under these same exposure conditions.

A satisfactory response was obtained with the positive control substances.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document : Attachment 5.5a.doc

Conclusion: Under the conditions of the test, PDC increased the

occurence of SCEs in CHO cells both in the absence and in

the presence of rat S9.

Reliability : (2) valid with restrictions

Comparable to guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Type : Ames test

System of testing : Salmonella typhimurium TA1535, TA100, TA1537, TA98

Test concentration : 31.5-3150 nl/plate in Standard plate test, 0.3-10 ml/20l desiccator

Cycotoxic concentr.

Result

Metabolic activation: with and without

 Result
 : negative

 Method
 : other

 Year
 : 1979

 GLP
 : no

Test substance : as prescribed by 1.1 - 1.4

Remark: no additional information

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (198)

Type : Ames test

System of testing : Salmonella typhimurium TA 100, TA 1535

Test concentration : 11500 ug/plate

Cycotoxic concentr.

Metabolic activation : with and without

Result : positive

Method : other: Ames Test

Year : 1975
GLP : no data
Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : Ames test

System of testing : Salmonella typhimurium TA 98, TA 1537, TA 1538

Test concentration : 33 - 2000 ug/plate

Cycotoxic concentr.

 Metabolic activation
 : with and without

 Result
 : negative

Method : other: Ames Test

Year : 1975
GLP : no data
Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : Ames test

System of testing : Salmonella typhimurium TA 100, TA 1535

Test concentration: 10000 - 50000 ug/plate

Cycotoxic concentr. :

Metabolic activation: with and without

Result : positive

Method : other: Ames Test

Year : 1975 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (200)

Type : Ames test

System of testing : Salmonella typhimurium TA 100

Test concentration : 113 - 11130 ug/plate

Cvcotoxic concentr. :

 Metabolic activation
 : with and without

 Result
 : negative

Method : other: Ames Test

Year : 1975
GLP : no data
Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (201)

Type : Escherichia coli reverse mutation assay

System of testing : Escherichia coli WP2s
Test concentration : 7.05 - 7224 ug/ml

Cycotoxic concentr.

Metabolic activation: with and without

Result : negative

Method : other: Prophage Lambda Induction Test

Year : 1990 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (202)

Type : DNA damage and repair assay
System of testing : Salmonella typhimurium TA 1535

Test concentration : 476 ug/ml

Cycotoxic concentr.

Metabolic activation: with and without

Result : negative

Method : other: Umu-Test

Year : 1985 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (203)

Type : Sister chromatid exchange assay

System of testing : V79 cells
Test concentration : 11.3 - 113 ug/ml

Cycotoxic concentr. :

Metabolic activation: with and withoutResult: positiveMethod: other: SCE-Test

Year : 1987 GLP : no data

Test substance : other TS: purity > 99 %

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (204)

Type : DNA damage and repair assay

System of testing : Escherichia coli PQ37

Test concentration : <= 2700 ug/ml

Cycotoxic concentr.

Metabolic activation : with and without

Result : negative

Method : other: SOS-Chromotest

Year : 1985 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (205)

Type : Bacterial gene mutation assay
System of testing : Streptomyces coelicolor
Test concentration : 2315 - 115600 ug/plate

Cycotoxic concentr.

Metabolic activation : without Result : negative

Method : other: Plate Incorporation Test

Year : 1978 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : Bacterial gene mutation assay
System of testing : Streptomyces coelicolor

Test concentration : 115600 ug/plate

Cycotoxic concentr.

Metabolic activation: withoutResult: negativeMethod: other: Spot Test

Year : 1978 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : other: Gene mutation in Aspergillus nidulans
System of testing : Aspergillus nidulans haploid strain 35

Test concentration: 115600 - 462400 ug/plate

Cycotoxic concentr.

Metabolic activation: withoutResult: positive

Method : other: Plate Incorporation Test

Year : 1980
GLP : no data
Test substance : no data

Remark: 8-Azaguanine resistance

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : other: Gene mutation in Aspergillus nidulans
System of testing : Aspergillus nidulans haploid strain 35

Test concentration: 346800 ug/plate

Cycotoxic concentr.

Metabolic activation: withoutResult: positiveMethod: other: Spot Test

Year : 1980 GLP : no data Test substance : no data

Remark : 8-Azaguanine resistance

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (199)

Type : Unscheduled DNA synthesis

System of testing : Human lymphocytes Test concentration : 1130 - 113000 ug/ml

Cycotoxic concentr. :

Metabolic activation: with and without

Result : negative

Method : other: DNA Damage and Repair/Unscheduled DNA-Synthesis

Year : 1983 GLP : no data Test substance : no data

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (206)

Type : Ames test

System of testing : Salmonella typhimurium TA1535, TA100, TA1537, TA98

Test concentration : $20-5000 \mu g/plate$ in Standard plate test, $3000-6000 \mu l/30l$ desiccator in the

modified test

Cycotoxic concentr. :

Metabolic activation: with and without

Result : positive

Method : other: Standard plate test and desiccator-Test (modified test)

Year : 1985 **GLP** : no

Test substance: as prescribed by 1.1 - 1.4

Remark: In the standard plate test only a light mutagen effect was

found, in the desiccator-test the substance was clearly

positive; no additional information.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (207)

Type : DNA damage and repair assay
System of testing : E. coli W3110/polA+, p3478/polA-

Test concentration : 2-20 µl/plate

Cycotoxic concentr. :

Metabolic activation: with and without

Result : negative

Method : other: according to Slater et al., J Bacteriol, 89, 1354-69

Year : 1971 **GLP** : no

Test substance: as prescribed by 1.1 - 1.4

Remark: no additional information

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (208)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay

Species: mouseSex: maleStrain: CD-1Route of admin.: gavageExposure period: 48 hr

Doses : 0, 150, 300 or 600 mg/kg bwt/d

Result : negative

Method : EPA OPPTS 870.5395

Year : 2003 GLP : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Range-finding Test:

Selection of the high-dose level for the definitive study was base upon results from a range-finding test where male and female mice (4/group) were administered up to 2000 mg/kg/day 1,2 dichloropropane by oral gavage in corn oil on two consecutive days. The animals were observed for 72 hr after the second dose, and decedents were subject to necropsy in an effort to determine the cause of death. Substantial drops in body temperature occurred 2 hrs after dosing in animals receiving 1000 mg/kg/day and higher doses and all mice at these doses died prior to the end of the observation period.

Micronucleus Test:

Groups of six male CD-1 mice (approximately 32g, 9 weeks old) were given PDC (0, 150, 300, a nd 600 mg/kg) by oral gavage in corn oil on two consecutive days. Clinical observations and body temperature were monitored prior to dosing, 2 and 5 hrs post dosing and prior to sacrifice. Only males were used in this assay since there was no substantial difference in toxicity between sexes in the

range-finding test.

Cyclophosphamide (120 mg/kg bwt, gavage, approx. 24 hr before sacrifice) was used as positive control substance.

Animals (6/dose) were sacrificed 24 hours after the second treatment, and femoral bone marrow collected to evaluate the incidence of micronuclei (MN) in polychromatic erythrocytes (2000 PCE/animal). The proportion of PCE among erythrocytes in the bone marrow was estimated by examining 200

in the bone marrow was estimated by examining 200

erythrocytes/animal.

Statistics

The raw data on the counts of MN-PCE for each animal were first transformed by adding one (1) to each count and then taking the natural log of the adjusted number. The

taking the natural log of the adjusted number. The transformed MN-PCE data and the data on percent PCE were analyzed separately by one-way ANOVA (Winer, B. J. (1971), Statistical Principles in Experimental Design (2nd Edition), McGraw-Hill, New York, New York). Pairwise comparisons of treated vs. control groups were done, if the dose effect was significant, by Dunnett's t-test, one-sided (upper) for MN-PCE and two-sided for the percent PCE (Winer 1971). Linear dose-related trend tests were performed only if any of the pairwise comparisons yielded significant differences. The alpha level at which all tests were conducted was 0.05.

Remark: Section 5.0 (Toxicokinetics) demonstrates widespread

distribution of PDC within the body, confirming contact with

the target tissue in this study.

Result : All animals survived until the end of the observation

period. Incoordination was observed in one mouse from the high-dose group. A uniform drop in body temperature (approx. 2°C) occurred 2 hrs postdosing in the high-dose

animals.

There was no statistically significant increase in the frequencies of MN-PCE in groups treated with PDC when compared to the negative controls. In contrast, a

significant increase in the frequency of MN -PCE was recorded

in the positive control group.

The mean proportion of PCE among bone marrow erythrocytes (200/animal) was unaffected by exposure to the test material while the positive control treatment significantly reduced this value.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : 1,2 dichloropropane was negative for the induction of

micronuclei in this test system under the experimental

conditions used.

Reliability : (1) valid without restriction

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (209)

Type : Dominant lethal assay

Species : rat Sex : male

Strain: Sprague-DawleyRoute of admin.: drinking water

Exposure period : 14 wk

Doses : 0, 0.024%, 0.10% or 0.24% (equivalent to 0, 28, 91 or 162 mg/kg bwt/d)

Result : negative

Method : other: 40 CFR 789.4700

Year : 1989 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method : Animals and treatments

PDC was administered in drinking water (0, 0.024%, 0.10% or 0.24%) to groups of 30 male SD rats (age 4 wk) for at least 13 wk as part of the breeding phase of a reproduction study (reported in Section 5.8.3). Treatment then ceased, and 2 days later each male was co-housed with two naive females/wk

for 2 wk.

The females were sacrificed by carbon dioxide inhalation approx. 14 days from the middle of their respective breeding period, and the numbers of corporea lutea, implantations and resorptions were recorded. No separate classification of early or late resorptions was performed. The uteri of apparently non-pregnant animals were stained with sodium sulphide solution (10%) and examined for evidence of early resorption sites.

A positive control group of 30 males received cyclophosphamide (100 mg/kg bwt in saline, by gavage) 48 hr prior to mating.

GC analysis showed that the test material was 99.9% pure. Stability testing demonstrated no degradation of aqueous solutions of PDC over 8 days. Based on these findings the experimental solutions were mixed and changed at least once per week, and analysed (GC) on at least 3 occasions prior to mating.

Statistics

Body weights were evaluated using Bartlett's test for equality of variances, followed by parametric or non-parametric ANOVA. If results of the ANOVA were positive, a Dunnett's test or Wilcoxon Rank-Sum test was performed. Fertility indices were analysed by the Fisher exact probability test. The numbers of corporea lutea were analysed using non-parametric ANOVA followed by the Wilcoxon Rank-Sum test. Pre-implantation losses and resorption rates were analysed by the Wilcoxon test.

Interpretation of findings

Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological and pathological findings. This appears scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study.

: General

Analysis of drinking water showed that the achieved concentration was 88%, 98% and 100% of nominal for the low, mid and high exposure groups, respectively (mean of 3 determinations).

In-life observations

There were no significant clinical effects noted in any treatment group during the in-life phase, however two animals from the low dose group died during the pre-breeding phase (test days 56 and 101; deaths ascribed to renal failure unrelated to treatment). Body weights for the high dose males were significantly decreased from day 8 of the study, while values for mid-dose animals were numerically (but not significantly) lower than control. Water consumption was decreased in a treatment-related manner (decreased by approx. 40-50%, 22% and 10% for the high, mid and low dose groups, respectively), and food intake lowered in high dose animals during the first week of the test.

Result

Seven of the 30 positive control group died, and one was sacrificed in a moribund state, during the breeding phase. Body weights and food and water consumption for these cyclophosphamide-treated animals were comparable to control values.

Received dose

Based upon body weight and water intake data, weekly average received doses were calculated as 0, 28.0, 90.7 and 162.1 mg/kg bwt/day for the 0%, 0.024%, 0.10% and 0.24% groups, respectively.

Mating and fertility indices

Mating performance and conception indices among treated males was comparable to control, ranging from 96.4% to 100%. These fertility parameters for cyclophosphamide-treated males were decreased significantly.

The number of corpora lutea from females mated with low and high dose was significantly increased during the first week of breeding, while the number of implantations for the second week of breeding was significantly lower in females mated with mid dose males. These differences appear consistent with normal biological variabiliy rather than any treatment-related effect. The number of pre-implantation losses was significantly higher in the low and high dose groups during the first week of treatment, however the values were essentially identical to the rate of pre-implantation loss observed in controls during the second week and therefore appeared unrelated to treatment. Similarly, resorption rates among these same treatment groups were significantly higher than control, but values from the second week of mating were similar to controls. Further details are presented in Attachment 5.6a.

Litter sizes, number of corporea lutea and number of implantations in the positive control group were significantly lower than control values, with a 2-fold increase in pre-implantation loss during the second week of breeding, and a 10-fold increase in resorption rates during both phases of mating.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Attached document: Attachment 5.6a.doc

Conclusion : PDC was not mutagenic at doses up to 0.24% in drinking water

(162 mg/kg bwt/day) when administered to male SD rats for 14

wk.

Reliability : (1) valid without restriction

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (210)

Type : Drosophila SLRL test
Species : Drosophila melanogaster

Sex: no dataStrain: no dataRoute of admin.: inhalationExposure period: 4 hoursDoses: 33840 ug/m3

Result

Method : other: Sex-linked Recessive Lethal Test in Drosophila melanogaster

Year : 1984 GLP : no data

Test substance : no data

Result : negative

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (211)

Type : Somatic mutation assay

Species: ratSex: no dataStrain: no dataRoute of admin.: inhalationExposure period: 3 daysDoses: 2200 mg/m3

Result

Method : other: Aneuploidy Test

Year : 1977
GLP : no data
Test substance : no data

Result : positive

The number of mononuclear and binuclear hepatocytes

containing polyploid nuclei (8 and 16 times

chromosomes/cell) increased compared to the control

group.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (212)

5.7 CARCINOGENICITY

Species : rat

Sex: male/femaleStrain: Fischer 344Route of admin.: gavageExposure period: 103 wkFrequency of treatm.: 5 d/wk

Post exposure period

Doses : males 0, 62 or 125 mg/kg bwt/d; females 0, 125 or 250 mg/kg bwt/d

Result

Control group : yes, concurrent vehicle

Method : other: standard NTP gavage study

Year : 1986 **GLP** : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female F344/N rats (4-6 wk old) were purchased from a commercial supplier, quarantined for 3 wk then randomly assiged to one control and two treatment groups (n = 50/sex/group). Males were treated with 0 (corn oil), 62 or 125 mg PDC/kg bwt/d, 5 d/wk for 103 wk by gavage. Females received 0, 125 or 250 mg/kg bwt/d over the same period. The dosing volume was 3 ml/kg bwt/d (hence stock dosing solution concentrations were 21 mg/ml, 42 mg/ml and 83 mg/ml for the 62, 125 and 250 mg/kg bwt treatments). Dosing solutions were

stored at 0-5 degrees C in dark glass bottles for up to 10 days.

Test sample, stability and achieved concentration Reagent grade PDC was used, with a purity of 99.4% (GC analysis). Toluene (0.24%) was identified as an impurity (GC/MS). GC-FID analysis demonstrated that 5.7% PDC in corn oil was stable at 25 degrees C for 7 days (recovery = 100% +/- 4%). Duplicate aliquots of the dosing solutions were analysed by GC-FID on 15 occasions during the study. Overall mean recoveries were 95%, 99% and 100% for the 21, 42 and 83 mg/ml solutions, respectively.

Observations

All animals were observed twice daily for signs of morbidity or mortality. Body weights were recorded weekly for the first 13 wk, then monthly thereafter. Moribund animals and all animals that survived to the end of the study were killed and necropsied. Thirty-one major tissues were examined, sampled and processed for histopathological examination.

Histopathological findings

Tissue slides, animal data and summary records were sent to a quality assurance laboratory for independent verification of the diagnoses of the study pathologist. All tumor diagnoses, target tissues and tissues from a randomly-selected 10% of the animals were subject to this assessment. Slides from all target tissues, plus those where the study pathologist and independent pathologist disagreed, were sent for further independent evaluation by a panel of NTP pathologists. The reported findings therefore represent a consensus from these various experts.

Statistical methods

Survival probabilities were estimated using Kaplan-Meir plots, and any treatment-related effect on survival analysed using the method of Cox. Analysis of tumor incidence data used Mantel and Haenszel contingency tables, and included pair-wise comparisons of low or high dose data versus control incidence plus an analysis of overall dose-response trends. Two methods were applied to animals dying before the end of the study. The first (life table analysis) assumed that all tumors of a given type were 'fatal' ie that they directly or indirectly were responsible for the death of the animal. Using this approach the proportion of tumor-bearing animals in the test and control groups were compared every time an animal died of a tumor of interest. The second method (incidental analysis) assume that all tumors observed before 103 wk were 'incidental', and the proportion of animals with tumors compared at 0-52 wk, 53-78 wk, 79-92 wk, wk 93-wk before terminal kill and the terminal kill. The Fisher exact test for pairwise comparisons and the Cochoran-Armitage linear trend test for dose-response effects were applied to the tumor data.

Remark

Based on tumor findings, NTP concluded that there was no evidence for the carcinogenicity of PDC in male rats, while in females treated with 250 mg/kg bwt/d for 103 wk NTP concluded there was equivocal evidence of an effect based upon a marginal increase in the incidence of mammary adenocarcinomas concurrent with decreased survival and

reduced body weight gain.

A historical incidence of 2% (3/150) was reported for the laboratory conducting this study, with an overall historical incidence of 1.2% (11/895)

Reduced survival and reduced body weight could indicate that treatments exceeded the Maximum Tolerated Dose in female rats.

: Body weight and clinical signs

Treated animals showed a dose-related reduction in body weight. Final body weights were approx. 5% lower than control for low dose animals, and 14% and 24% lower then control in the high dose male and female groups, respectively. (Female body weight was decreased by >20% from wk 76 of the study.) No clinical signs are described.

Survival

The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.001) below that of the low dose females and controls (32%, 86% and 74% survival to the end of the study). Mortality and morbidity were especially marked at wk 94 of the study. Survival in males was comparable for all groups (78%, 84% and 82% alive at wk 103 for the control, 62 mg/kg bwt/d and 125 mg/kg bwt/d groups, respectively).

Tumor pathology

Because of reduced survival in high dose female rats, statistical procedures that adjust for intercurrent mortality (life table and incidental tumor tests) were regarded as more meaningful than the 'unadjusted' analysis.

A quantitative increased tumor incidence in one or both treatment groups relative to control, or a positive trend in the absence of any statistically significant difference between the treated and control groups, was seen for the following tissues and tumor types:

* mammary gland

mammary gland hyperplasia was increased, and there was a positive trend for mammary adenocarcinoma (adjusted rates: 2,7%, 4.7%, 26.7%; significantly increased in high dose group), both in females only; the overall incidence of fibroadenomas showed a negative trend in females. Tumor incidence in the high dose group was strongly influenced by findings in 4 of 16 animals that survived to the end of the study. A historical incidence of 2% (3/150) was reported for the laboratory conducting this study, with an overall historical incidence of 1.2% (11/895).

* uterus

enometrial stromal polyps occurred with a significant positive trend, although the incidence in the individual treatment groups was not increased relative to control.

* thyroid

follicluar cell carcinoma were found in two low dose females (but not in control or high dose females) at study termination; historic range 0.2-0.7%.

* stomach or forestomach a non-significant increase in squamous cell papillomas was

Result

found in two high dose females (none in control); historic range 0-0.3%.

* pancreas

islet cell carcinomas occurred with a positive trend in males, however the incidence of adenomas was greatest in the control group and the combined incidence (adenoma + carcinomas) was not different between the groups.

* pituitary

while the incidence of adenomas was significantly increased in low dose females, the survival-adjusted incidence was unremarkable; the incidence of pituitary carcinomas was greatest in control females; the incidence of combined (adenomas + carcinomas) was not increased significantly.

* adrenal glands

pheochromocytomas showed a negative trend in males, and there was no difference in the incidence in combined pheochromocytoma + malignant pheochromocytoma).

No tumors were present in liver, a tissue showing signs of non-neoplastic changes (see above).

Note: Significant increases were observed in virus antibody titers. The report notes that the relationship between these increases and occurrence of non-neoplastic and neoplastic changes in unclear.

changes is unclear.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : NTP concluded that under the conditions of this study there was no evidence that PDC was a carcinogen in male rats

treated by gavage at doses up to 125 mg/kd bwt/d or 250 mg/kg bwt/d, respectively, for up to 103 wk. There was equivocal evidence of an increase in mammary tumors in high

dose females, but no other tissues were affected.

Reliability : (1) valid without restriction

Comparable to guideline study, with restrictions.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

Species: mouseSex: male/femaleStrain: B6C3F1Route of admin.: gavageExposure period: 103 wkFrequency of treatm.: 5 d/wk

Post exposure period

Doses : 0, 125 or 250 mg/kg bwt/d

Result

Control group : yes, concurrent vehicle

Method: other: standard NTP gavage study

Year :

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female B6C3F1 mice (4-6 wk old) were purchased from a commercial supplier, quarantined for 3 wk then randomly

assiged to one control and two treatment groups (n =

50/sex/group). They were given 0, 125 or 250 mg PDC/kg bwt/d 5 d/wk for 103 wk by gavage. The dosing volume was 3 ml/kg bwt/d (hence stock dosing solution concentrations were 21

mg/ml, 42 mg/ml and 83 mg/ml for the 62, 125 and 250 mg/kg bwt treatments). Dosing solutions were stored at 0-5 degrees C in dark glass bottles for up to 10 days.

Test sample, stability and achieved concentration Reagent grade PDC was used, with a purity of 99.4% (GC analysis). Toluene (0.24%) was identified as an impurity (GC/MS). GC-FID analysis demonstrated that 5.7% PDC in corn oil was stable at 25 degrees C for 7 days (recovery = 100% +/- 4%). Duplicate aliquots of the dosing solutions were analysed by GC-FID on 15 occasions during the study. Overall mean recoveries were 95%, 99% and 100% for the 21, 42 and 83 mg/ml solutions, respectively.

Observations

All animals were observed twice daily for signs of morbidity or mortality. Body weights were recorded weekly for the first 13wk, then monthly thereafter. Moribund animals and all animals that survived to the end of the study were killed and necropsied. Thirty-two major tissues were examined, sampled and processed for histopathological examination.

Histopathological findings

Tissue slides, animal data and summary records were sent to a quality assurance laboratory for independent verification of the diagnoses of the study pathologist. All tumor diagnoses, target tissues and tissues from a randomly-selected 10% of the animals were subject to this assessment. Slides from all target tissues, plus those where the study pathologist and independent pathologist disagreed, were sent for further independent evaluation by a panel of NTP pathologists. The reported findings therefore represent a

consensus from these various experts.

Statistical methods

Survival probabilities were estimated using Kaplan-Meir plots, and any treatment-related effect on survival analysed using the method of Cox. Analysis of tumor incidence data used Mantel and Haenszel contingency tables, and included pair-wise comparisons of low or high dose data versus control incidence plus an analysis of overall dose-response trends. Two methods were applied to animals dving before the end of the study. The first (life table analysis) assumed that all tumors of a given type were 'fatal' ie that they directly or indirectly were responsible for the death of the animal. Using this approach the proportion of tumor-bearing animals in the test and control groups were compared every time an animal died of a tumor of interest. The second method (incidental analysis) assume that all tumors observed before 103 wk were 'incidental', and the proportion of animals with tumors compared at 0-52 wk, 53-78 wk, 79-92 wk. wk 93-wk before terminal kill and the terminal kill. The Fisher exact test for pairwise comparisons and the Cochoran-Armitage linear trend test for dose-response effects were applied to the tumor data.

: The liver was the principal target for PDC toxicity in the mouse, with hepatocytomegaly and hepatic focal necrosis seen in male mice only. It was also the key site for tumor

formation.

Remark

Hepatocellular adenoma is a common finding in control B6C3F1 mice. Historic control data for this lesion in NTP studies conducted to 1995 (corn oil gavage, 16 studies) returned an incidence of 267/813 or 33% in males, with a range of 14-58%; equivalent values for females were 111/809 = 14%, with a range of 2-28% (Source: Analytical Services Inc. (1995) Tumor Incidence in Control Animals by Route and Vehicle of Administration: B6C3F1 Mice. prepared for NIEHS, 6 June 1995).

Comparison of this historic control information with findings from the NTP leads to the following conclusions:

* The control incidence of hepatocellular adenoma for male (20%) and female (3%) mice from this NTP study was markedly

- lower than the mean historic incidence (33% in males; 14% in females);
- males (45%) was within the spontaneous range (14-58%);

 * The incidence of hepatocellular adenoma in low- (17%) and high dose (19%) female mice was also within the spontaneous range (2-28%);
- * Liver tumor incidence in both sexes appeared non-linear when related to received dose.

* The incidence of hepatocellular adenoma in high dose

Body weight and clinical signs
Mean body weights of treated and vehicle control animals
were comparable, and no compound-related clinical signs were
noted.

Survival

The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.035) less than that of the low dose females and controls, with 70%, 58% and 52% of the control, low and high dose animals surviving to termination. Survival in males was comparable for all groups (70%, 66% and 70% alive at wk 103 for the control, 125 mg/kg bwt/d and 250 mg/kg bwt/d groups, respectively). The report notes that the lowered survival in female mice was related to an increased incidence of reproductive tract infections in animals which died before the end of the study (45% of controls affected versus 64% of both the low and high dose females that died during the study).

Non-tumor pathology

Hepatocytomegaly (6%, 10% and 30% for control, low dose and high dose animals, respectively) and hepatic focal necrosis (4%, 10% and 20%) were seen in male mice only. Acanthosis of the surface epithelium of the forestomach occurred at increased incidence in high dose males (0%, 0%, 4%) and both groups of treated females (0%, 10%, 8%). Suppurative inflammation (affecting ovary, uterus or multiple organs) was found in 5/11 control, 9/14 low dose and 14/22 high dose females that died before the end of the study.

Tumor pathology

Tumors were found in the following tissues, although the increase was not always statistically significant and/or dose-related:

* liver

There was a positive trend for liver adenomas in male (20%, 29%, 45%, adjusted for intercurrent mortality) and female (3%, 17%, 19%, adjusted) mice. Tumor incidences in high dose

Result

males (P=0.017, lifetable test) and both low (0.064, lifetable test) and high dose (P=0.047, lifetable test) females were increased significantly relative to control.

* thyroid

Two high dose females had follicular cell carcinomas, and 3 had follicular cell adenomas. The combined incidence of adenomas or carcinomas in high dose females (21% adjusted) was increased significantly (P=0.040, lifetable test) relative to the controls (3% adjusted), with a historical rate of 1%-3.8%. There were no tumors in the controls.

* forestomach

Squamous cell papillomas occurred at an incidence of 0%, 2% and 6% in control, low dose and high dose male mice, and at 0%, 4% and 4% in the equivalent female groups. Historical rates for this tumor are in the range 0-0.2% for male B6C3F1 mice and 0-0.3% for females. One high dose female had a squamous cell papilloma (2% incidence, historical range of 0-0.3%).

* lung

Alveolar/bronchiolar adenomas and alveolar/bronchiolar adenomas or carcinomas (combined) showed a significant negative trend in female mice.

* external surface

Subcutaneous fibromas or fibrosarcomas and fibromas or fibrosarcomas of the skin or subcutaneous tissue occurred with a significant negative trend in male mice.

Note: Significant increases were observed in virus antibody titers. The reports notes that the relationship between these increases and occurence of the non-neoplastic- and neoplastic changes is unclear.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion : NTP concluded that under the conditions of this study PDC

increased the incidence of hepatic adenomas in B6C3F1 mice treated with 125 mg/kd bwt/d or 250 mg/kg bwt/d by gavage

for up to 103 wk.

Reliability : (1) valid without restriction

Comparable to guideline study, with restrictions.

Flag : Critical study for SIDS endpoint

25.10.2004 (186)

5.8.1 TOXICITY TO FERTILITY

Type : Two generation study

Species : rat

Sex: male/femaleStrain: Sprague-DawleyRoute of admin.: drinking waterExposure period: 41 wk (f0 adults)

Frequency of treatm. : daily

Premating exposure period

Male : 10 - 14 wk Female : 10 - 14 wk

Duration of test :

No. of generation : 2

studies

Doses : 0.024%, 0.10%, 0.24% Control group : yes, concurrent vehicle

 NOAEL parental
 : = .024 %

 NOAEL F1 offspring
 : = .1 %

 NOAEL F2 offspring
 : = .1 %

 other: reproduction
 : = .24 %

NOEL Method

: EPA OTS 798.4700

Year : 1990 **GLP** : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Animals and treatments

Male and female SD rats were purchased at 4 wk of age from a commercial supplier, stratified by weight and randomly assigned to treatment groups upon receipt. After two weeks acclimatization, PDC was administered in drinking water at concentrations of 0 (control), 0.024%, 0.10% or 0.24%

(w/v).

Preparation of dosing solutions

The high dose exposure concentration was selected based upon the theoretical maximal solubility of PDC in water (ie 0.27 g/100 ml). Stability testing showed that >90% of the initial concentration of high dose solution was recovered after 21 days, therefore fresh solutions were prepared at weekly intervals. The lower exposure concentrations were prepared by dilution of the 0.24% solution. All dosing solutions were administered to the animals using sealed Tedlar gas and water sampling bags, fitted with a pressure-activated stainless steel nipple, in order to minimise losses by volatilization. All dosing solutions were analysed on at least 3 occasions per generation during the study. (Note: the analytical method used is not stated, however a limit of detection of 3.08 - 10.1 ug/ml is reported.)

Experimental design

The f0 generation comprised 30 male and 30 female rats per group, and treatment commenced at 6 wk of age. After approx. 10 wk treatment, f0 animals were mated (one male to one female) to produce the f1 litters. Following weaning (3 wk old), 30 males and 30 females from the f1 litters were randomly selected to be the parents of the next generation. Following approx. 12 wk treatment, the f1 adults were mated to produce the f2 litters. For the f1 mating, cohabitation of male and female littermates was avoided.

To reduce variation in pup growth, f1 and f2 litters with greater than 8 pups were reduced in size on PND 4 to 4 males and 4 female. Litters with 8 or fewer pups were not culled. Weaning of all litters occurred 3 weeks after delivery.

Further details of the experimental design are given in Attachment 5.8.1a.

Parental observations

Body weight and food and water consumption were recorded weekly in males and in females pre-parturition, and at 3 day intervals in females post-parturition. f0 and f1 adults were subject to a complete necropsy after the last litter from

each generation had been weaned. Liver, kidney and a representative range of other tissues were weighed, sampled and preserved. Bone marrow, coagulating glands, epididymides, kidneys, ovaries, oviducts, pituitary, prostate, seminal vesicles, testes, uterus, vagina and any abnormal gross lesions from the control and high dose groups (f0 and f1) were processed and examined by light microscopy. Hematology parameters (hematocrit, hemoglobin concentration, red cell count, total white cell count, platelet count, red cell morphology) were determined in f0 and f1 animals using blood collected from 10 rats/sex/dose level at necropsy.

Litter observations

All litters were examined as soon as possible after delivery, and parturition date, litter size, weight and sex of each pup and number of live and dead pups on PND 0-21 recorded. Any physical abnormalities at birth or during lactation were recorded.

Weanling observations

10 pups/sex/dose level from the f0 and f1 generations were randomly selected for necropsy at weaning. Liver and kidney weights were recorded, and hematology parameters determined (same details as adults). Tissues were sampled and preserved, but not subject to histopathological assessment.

Statistics

Body weights, organ weights, litter size, hematology and gestation data were evaluated by Bartlett's test for equality of variances, followed by either parametric or non-parametric ANOVA. If the ANOVA was significant, a Dunnett's test or the Wilcoxon Rank-Sum test with Bonferroni's correction was performed. Descriptive statistics were reported for food and water consumption. Fertility indices were evaluated by the Fisher exact probability t est and neonatal sex ratios analysed by the binomial distribution test. Survival indices and other neonatal incidence data were analyzed using the litter as the experimental unit.

Result

Analysis of dosing solutions and received dose Mean exposure concentrations (determined on 3 -4 occasions and presented as percent nominal with SD in parentheses) for the low, mid and high dose groups were as follows: f0 males: 88.8 (6.1), 98.2 (7.3), 100.0 (8.2) f0 females: 90.3 (6.9), 100.4 (4.3), 102.4 (8.4) f1 males: 100.7 (29.0), 96.0 (0.9), 95.3 (2.2)

GENERAL

See Attachment 5.8.1 summary.doc for an overview of the main findings from this study.

PARENTAL GENERATIONS

Received dose

Based upon mean body weight and water consumption data, males of both generations from the low, mid and high dose groups received approx. 20 - 30, 70 - 130 and 130 - 250 mg/kg bwt/d. Equivalent female groups received 30 - 40, 110 - 140 and 190 - 270 mg/kg bwt/d. Female water consumption increased during lactation, with received doses of approx 60, 200 450 - 500 mg/kg bwt/d. Further details are presented

f1 females: 94.6 (21.8), 97.7 (2.6), 96.1 (3.1)

in Attachment 5.8.1b.

In life observations

No treatment-related clinical signs were observed.

Food consumption

There were relatively minor and sporadic effects on food intake. f0 females from the high and low dose groups consumed 10% and 6% less than the controls, while f1 males from the high dose group showed an overall 8% reduction in food consumption (pre-mating and mating phases). Food intake data for the other groups were generally unremarkable.

Water consumption

A dose-related decrease in water consumption was apparent in animals from both the f0 and f1 generations, presumably reflecting reduced palatability in the mid and high dose groups. Overall, water consumption in high dose males and pregnant females was 50-60% of control, and 70% of control in lactating females. Water intake in mid dose males and mid dose pregnant females was 70 - 80% of control, and 75 - 85% of control consumption in mid dose lactating females. Results for the low dose animals were 90 - 104% of control.

NOTE: Water consumption typically increases from around gestation day 13 in order to compensate for increased plasma and extracellular fluid volumes during the late stages of pregnancy. This was not the case in this study, due to the unacceptable palatability of the drinking water. This would be expected to have an adverse influence on fetal development. It is also pertinent that water consumption in untreated (control) females increased in this study during lactation, whereas major reductions were apparent in treated animals during lactation. This would be expected to have impacted post-natal survival of the pups.

Parental body weight

Body weights for the high dose ani mals were significantly (alpha = 0.05) lower than control in f0 and f1 generations of both sexes. In terms of affecting reproductive outcomes, effects in females appeared particularly important. Thus body weights for high dose f0 and f1 females were 5% and 11% lower than control during the pre-mating period, with a 10-12% decrement present during gestation and an approx. 15% reduction during lactation. Gestation body weight gains were decreased by approx. 20% in f0 and f1 females given 0.24% PDC, and by 7-13% in females given 0.1% PDC. Less consistent body weight decrements were noted in the mid dose animals, with negligible effects in the low dose generations.

Reproductive indices

There were no significant or obvious treatment-related differences in male or female reproductive performance, as assessed from mating-and conception indices, fertility or gestational period. Sporadic differences seen for some female parameters were not dose-related (ie present in low and/or mid but not high dose animals) or were within the range of historic control data. All females produced viable litters.

Hematology

Sporadic hematological changes noted in this study were not

dose related and inconsistently expressed in males and females of the same generation and in same sex animals of different generations. Overall these effects appeared incidental and unrelated to treatment with PDC.

Necropsy observations

Increased relative kidney weight values in high dose animals (both sexes) appeared secondary to a lower terminal body weight. No gross pathological changes were noted in any of the parental animals.

Histology

Treatment-related histologic changes were limited to increased hepatocellular granularity (adaptive change) in males and females of both generations at all dose levels. Although no statistical analyses are reported, the incidence in high dose females (17% and 10% for f0 and f1, resectively) and high dose f1 males (13%) appears greater than control (0 - 2% for all sex/generation groups). The response in f1 high dose males (5% incidence) and mid and low dose animals of the other generations were less pronounced (2 - 8% incidence) and/or not dose related. All other tissues, including reproductive organs from both sexes, were unremarkable.

LITTER DATA

There were no significant treatment-related external observations or difference in sex ratio in either generation. The number of pups born alive was similar in the control and test groups from both phases of the study, however postnatal survival in high dose f1 litters was significantly lower than control while that of the high dose f2 litters was 10% lower than controls on PND 14 and 21; these effects appeared treatment-related. Bodyweights for high dose f0 neonates were significantly decreased, with day 21 values approx. 15% lower than control. Bodyweights of f1 litters were less severely affected (4 - 7% reduction), and attained significance only on lactation day 21.

WEANLING DATA

An increased hemoglobin concentration in high dose f1 males and an increased mean relative kidney weight in high dose f1 females appeared related to a lowered water intake and body weight, respectively. All other hematological and gross necropsy observations were comparable to control in both the f1 and the f2 generations.

Source

Attached document

: The 1,2-Dichloropropane ICCA/HPV Consortium

: Attachment 5.8.1 summary.doc

Attachment 5.8.1a.doc

Attachment 5.8.1b.doc

Conclusion

Propylene dichloride was not a reproductive toxin when tested over 2 generations in SD rats exposed to 0.024%, 0.1% and 0.24% in drinking water.

Decreased water consumption (presumably reflecting unacceptable

palatability of the test solution) and lowered body weight, and increased hepatocellular granularity (adaptive change), were present in parental animals from the 0.24% groups of both generations. Neonatal growth and survival were decreased in the 0.24% treatment groups, probably in response to decreased maternal water intake and lower

growth. There was no effect on reproductive performance,

live births or litter size in any of the test groups.

Thus the NOAEL for adults and neonatal effects was 0.1% PDC while the reproductive NOEL was 0.24% PDC, the limit of

solubility.

Reliability : (1) valid without restriction

GLP auideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (213)

Type : Two generation study

Species : rat

Sex: male/femaleStrain: Sprague-DawleyRoute of admin.: drinking water

Exposure period : F0 males 20 weeks, F0 females 20 weeks F1 males 21 weeks, F1 females 21 weeks

Frequency of treatm. : daily

Premating exposure period

Male : F0 10 weeks, F1 12 weeks Female : F0 10 weeks, F1 12 weeks

Duration of test : 41 weeks

No. of generation

studies

Doses : 0.024, 0.10 and 0.24 % in drinking water

Control group : yes, concurrent no treatment

NOAEL parental : = .024 %NOAEL F1 offspring : = .1 %

Method : other: Two-generation Reproduction Toxicity Test

Year : 1988 **GLP** : ves

Test substance : as prescribed by 1.1 - 1.4

Remark: The F0-animals were exposed to 1,2-dichloropropane in

drinking water first for a period of 10 weeks before mating, then for a maximum 3 weeks during mating and finally during feeding of the young. The animals of the F1-generation were analogously treated. F2 animals were dosed until they were

21

days old; 30 animals/sex/dosage and control group.

Result : No influence (substance-related) on reproduction parameters

(fertility and brood parameters) was observed. The survival rate and the average body weight gain of the F1-young animals were significantly (p <= 0.05) decreased in the 0.24% dosage group from postnatal day 1 - 21 (10 % mortality, difference in body weight approximately 15 % compared to the control group). These changes were not considered as a direct toxic effect of 1,2-dichloroproane, but as a secondary effect of the reduced maternal drinking water consumption. No other substance-related changes were found in the analyzed organs of F0-and F1-animals (liver in all concentration groups; other reproductive organs, kidney, hypophysis and marrow in the high dosage group) other than the increase in hepatocellular granulation for all dose

groups.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (214)

ld 78-87-5 5. Toxicity Date 14.12.2004

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species rat Sex female

Strain Sprague-Dawley

Route of admin. gavage

Exposure period : GD 6 - 15 inclusive

Frequency of treatm. dailv

Duration of test

Doses 0 (corn oil), 10, 30 or 125 mg/kg bwt/d

Control group ves. concurrent vehicle NOAEL maternal tox. = 30 mg/kg bwNOAEL teratogen. = 125 mg/kg bw NOAEL Fetotoxicity = 30 mg/kg bwEPA OTS 798.4900 Method

Year 1995 GLP yes

Test substance as prescribed by 1.1 - 1.4

Method Animals and treatments

> Pregnant female SD rats (approx. 14 wk old, n = 30) were randomised into groups and administered PDC by gavage at doses of 0 (corn oil), 10, 30 or 125 mg/kg bwt/d on GD 6-

15 inclusive.

The concentration of PDC in the dosing solutions was verified using GC-FID.

Parental observations

Animals were observed daily in their cages, and also subject to a more intensive clinical examination 30 - 60 min post-dosing. This included observation of pupil size, respiration, movement (muscle tone, extensor thrust reflex, general behaviour, tremors, convulsions etc), condition of skin and haircoat (ie piloerection), salivation, lacrimation and any other abnormal events. Food and water intake was recorded every 2 - 4 days, and body weights on GD 0, 16 and 21. The dams were sacrified on GD 21, when liver, kidney, spleen and gravid uterine weights were recorded.

Fetal observations

The number of corpora lutea, the number and position of implantations and the number of live or dead fetuses were recorded. In addition, the sex and body weight of each fetus was recorded, and any gross external alterations recorded. At least one-half of each litter was examined immediately for visceral alterations, with subsequent evaluation of skeletal abnormalities using alizarin red-S.

The data were analysed intially using Bartlett's test, parametric or non-parametric ANOVA, Dunnett's test and the Wilcoxon Rank-Sum test. Pregnancy rates were analysed using the Fischer exact probability test, and fetal sex ratios evaluated using a binomial distribution test.

Interpretation of findings

Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological

and pathological findings. This is scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study

Result

Mean analysed concentrations of PDC were 5.0 (0.0), 15.0 (0.0) and 62.5 (2.0) mg/ml (SD in brackets).

Maternal observations

Clinical signs (ie decreased movement and muscle tone, increased lacrimation, decreased extensor reflex and increased salivation) were present in high dose animals on GD 6 and to a lesser extent on GD 7. Despite the transitory nature of these changes, they appeared indicative of an adverse effect in dams from the high dose group. No clinical effects were seen on other days in the high dose group, or on any day in the mid- or low dose animals.

Body weights were slightly (3-5%) but significantly lower in high dose dams throughout the study. Body weight gain was decreased significantly in high dose dams on GD 6-9, and although comparable to control during the mid- and latter stages of pregnancy the overall weight increase in the 125 mg/kg bwt/day group was approx. 30% lower than controls on GD 6-16 (that is, during the dosing period). Food consumption was reduced approx. 25% on GD 6-9, and water consumption increased by the same amount on GD 9-12 and 12-15.

There were no significant effects on absolute or relative organ weights, or on uterine weights or pregnancy parameters (including number of litters, corpora lutea per dam, implantations per dam, live fetuses per litter, resorptions, fetal bwt, etc).

Fetal observations

A low incidence of malformations was present in all groups, with no qualitative or quantitative increase in litters from treated dams. Overall there was no indication that PDC was a teratogen.

Fetal variations were present in both control and treated groups. The only treatment-related effect was a significant increase in the incidence of delayed ossification of the bones of the skull among fetuses from the high dose group. Interestingly, the occurrence of this observation was most common in high dose litters containing 16 or more pups. All other parameters were comparable to the controls.

Source Conclusion

- : The 1,2-Dichloropropane ICCA/HPV Consortium
- Under the conditions of the study, mild fetotoxicity (as evidenced by decreased ossification of the bones of the skull) was noted in litters from dams given 125 mg/kg bwt PDC/day. This effect was most common in the larger litters, and was co-incident with significant reductions in body weight gain and food consumption. It is concluded that the NOAEC for both maternal and fetal toxicity was 30 mg/kg bwt/day.

Reliability

(1) valid without restriction
 GLP guideline study.

Flag 25.10.2004

: Critical study for SIDS endpoint

(215)

Species : rabbit Sex : female

Strain : New Zealand white

Route of admin. : gavage

Exposure period : GD 7 - 19 inclusive

Frequency of treatm. : daily

Duration of test

Doses : 0 (corn oil), 15, 50 or 150 mg/kg bwt/ d

Control group : yes, concurrent vehicle

NOAEL maternal tox. : = 50 mg/kg bw

NOAEL teratogen. : = 150 mg/kg bw

NOAEL Fetotoxicity : = 50 mg/kg bw

Method : EPA OTS 798.4900

Year :

GLP : yes

Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments

Artificially-inseminated pregnant female New Zealand rabbits (approx. 6.5 mo old, n = 18) were randomised into groups and administered PDC by gavage at doses of 0 (corn oil), 15, 50 cr 150 mg/kg but/ d on CDZ 110 inclusive

or 150 mg/kg bwt/ d on GD 7 - 19 inclusive.

The concentration of PDC in the dosing solutions was verified using GC-FID.

Parental observations

Food and water intake was recorded every 2 - 4 days, and body weights on GD 0, 20 and 28. Blood samples were collected on GD 19 and subject to an extensive haematological examination. The dams were sacrified on GD 28, when liver, kidney, spleen and gravid uterine weights were recorded.

Fetal observations

The number of corpora lutea, the number and position of implantations and the number of live or dead fetuses were recorded. In addition, the sex and body weight of each fetus was recorded, and any gross external alterations recorded. All rabbit litters were examined immediately for visceral alterations, with subsequent evaluation of skeletal abnormalities using alizarin red-S.

Statistics

The data were analysed intially using Bartlett's test, parametric or non-parametric ANOVA, Dunnett's test and the Wilcoxon Rank-Sum test. Pregnancy rates were analysed using the Fischer exact probability test, and fetal sex ratios evaluated using a binomial distribution test.

Interpretation of findings

Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological and pathological findings. This appears scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study.

St

Result : Mean analysed concentrations of PDC were 14.8 (0.06), 49.4

(0.34) and 150.0 (1.94) mg/ml (SD in brackets).

Maternal observations

One rabbit from the high dose group died on GD 22 (ie after gavage treatment had ended) but no cause of death could be identified at necropsy. The remainder of the high dose dams exhibited intermittent anorexia (data not presented). There were no other significant changes in behaviour or demeanor among rabbits during the course of the study.

Body weight gain among the high dose dams was significantly lower than that of the controls (net loss of 165 g compared to a net gain of 49 g in the controls on GD 7-20), although absolute bwt appeared unaffected.

Haematological examinations demonstrated the clear effects in high dose dams (other groups unaffected), with red cell counts, haemoglobin concentration and haematocrit all decreased by 18-20% while platelet and white cell counts were increased 20-25%. The percentage of reticulocytes was approx. double in high dose animals when compared to the controls.

There were no significant effects on absolute or relative organ weights, or on uterine weights or pregnancy parameters (including number of litters, corpora lutea per dam, implantations per dam, live fetuses per litter, resorptions, fetal bwt, etc).

Fetal observations

There was no increase in the incidence of malformations in any of the treated groups when compared with the controls. Overall there was no indication that PDC was a teratogen.

Fetal variations were present in both control and treated groups. The only treatment-related effect was a significant increase in the incidence of delayed ossification of the bones of the skull among fetuses from the high dose group. All other parameters were comparable to the controls.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study PDC was not selectively

toxic to the fetus, causing a slight delay in ossification

of the fetal skull at doses causing systemic

(haematological) changes in the dams. The NOAEL for maternal

and fetal effects in the rabbit is 50 mg/kg bwt.

: (1) valid without restriction

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (215)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

Reliability

Endpoint : Neurotoxicity

Study descr. in chapter : Reference : Type : Species : rat

Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
No. of animals : 15

Vehicle : other: corn oil
Exposure period : 90 day(s)
Frequency of treatm. : 5 d/wk for 13 wk

Doses : 0, 20, 65 or 200 mg/kg bwt **Control group** : yes, concurrent vehicle

Observation period : 13 wk during treatment + 9 wk recovery period

Result : No gross or histopathologic changes in central or peripheral nervous

system

Method : other: functional observation battery = EPA 798.6050; motor activity =

EPA798.6200; neuropathology = EPA798.6400.

Year : 1988 **GLP** : yes

Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments

Male and female F344 rats (approx. 8 wk old; n=15/sex) were administered 0 (control, corn oil, 1ml/kg bwt), 20, 65 or 200 mg PDC/kg bwt/d via gavage, 5 d/wk for 13 wk (equivalent to a total of 65 treatments). Fresh dosing solutions were prepared monthly, and the concentration of PDC confirmed using GC.

A dose of 200 mg/kg bwt/d was chosen for the high dose group based on the known acute CNS effects of PDC ie this level of exposure was expected to significantly challenge the animals but not cause frank systemic toxicity.

After 13wk treatment, 4 rats/sex/dose were randomly selected for terminal examinations. The remainder were allowed a 9 wk recovery period, after all were sacrificed and 5 rats/sex/dose were taken for necropsy.

Cage side obs ervations were conducted twice daily. The animals were also subject to handling and observation at the time of dosing, and subjected to a detailed external examination each week.

Functional Observational Battery (FOB)

The animals were subjected to FOB evaluation before treatment commenced and at monthly intervals during the main study period. The observations were conducted by the same technician before the daily dosing. Endpoints included:

- *Observations in-hand
- pupil size
- respiration
- movement
- condition of skin and coat
- salivation
- lacrimation
- urine staining
- faecal staining
- * Observations in a clear plastic box
- locomotor behaviour
- responsiveness to touch
- responsiveness to sharp noise
- responsiveness to tail pinch
- visual placing

Grip strength

Hindlimb grip strength was measured before treatment commenced and at monthly intervals during the main study period. The test involved placing the rat's forelegs on a bench and the hindfeet on a horizontal screen attached to a strain gauge. The observer then smoothly but firmly pulled backward on the tail until the grip of the hind feet was broken. The strongest response from three trials was used for statistical analysis.

Motor activity

Motor activity was evaluated before treatment commenced and at monthly intervals thereafter in a doughnut-shaped plexiglass alley over five 8 min sessions. An infrared photo beam crossed the alley in two locations to record movement.

Body weight and temperature

Body weights were recorded weekly and also on the days when the FOB and motor activity assessments were conducted. Body temperature was recorded using a thermistor on the last day of dosing concurrently with the FOB.

Necropsy

Four rats/sex/dose level were fasted overnight prior to necropsy. The animals were given heparin prior to anesthesia, then sacrificed by whole body perfusion and fixing with gluteraldehyde/formaldehyde solution. A macroscopic examination (limited in extent by the perfusion process) was performed prior to removal of the brain and selected nervous system tissues. The liver, kidneys and spleen (possible target tissues) were sampled and preserved.

Histopathology

The following nervous system tissues from control and high dose animals were subject to the microscopic evaluation:

- brain (6 levels)
- spinal cord (cervical and lumbar)
- Gasserian ganglia
- dorsal and ventral spinal nerve roots
- dorsal root ganglia (cervical and lumbar)
- sciatic, tibial and sural nerves

Special stains were used to examine neuronal bodies, axons and neurofibrials and myelin.

Recovery phase

11 rats/sex/dose level were retained for possible further examination, pending preliminary assessment of fidnings from the main study. The animals were observed for clinical signs twice daily and subject to a more detailed external examination each week. Body weights were recorded weekly, and body temperature recorded 1, 2, 4 and 8 wk after treatment ended. Five rats/sex/dose were taken for necropsy after a 9 wk recovery period, the remainder were euthantized without further examination.

Statistical analysis

The data were subject to extensive statistical evaluation, including Bartlett's test, parametric and non-parametric ANOVA, Dunnett's test, Wilcoxon Rank-Sum test, Bonferroni correction, Outlier test, 2-way ANOVA. In view of the very large number of comparisons considered in this study, the final interpretation of the data considered results from

statistical analyses along with other factors such as dose-response relationships and whether the results were meaningful in the light of other findings.

Result : Dosing solutions

Analysis of the dosing solutions demonstrated that the concentration of PDC was at or slightly above the target, varying from 100 to 110.5% of nominal. There was no appreciable loss due to volatilisation (<6% decrease) and the PDC was distributed in a homogeneous manner within the master batch of each solution.

General

All rats survived the 13 wk treatment period. Clinical signs included lacrimation and blinking in a dose-dependent manner on the first day, with decreased spontaneous motor activity (for up to 4 hr post-treatment in the high dose group). No effect on motor activity was noticeable in the low- and mid dose groups by day 3, or in the high dose animals by day 4. No other treatment-related clinical signs were present.

Body weight

A significant decrease in body weight of high dose males was apparent during the first week of treatment which persisted throughout the 13 wk dosing period (6-10% reduction overall). Body weights of mid dose males were also decreased consistently and, although the change was not always significant, this was also considered to be treatment related by the authors of the study report. Body weights of high dose females were also slightly decreased (equivocal, non-significant effect). There was no effect on the body weights of low dose males or mid and low dose females.

FOB

No differences were apparent between control and treated animals at any of the test intervals.

Hind limb grip strength

The only statistically significant effect noted was an increase in grip strength in high dose animals (both sexes) 1 month following the start of treatment. This finding was not replicated 2 or 3 months into the study, and was considered coincidental to treatment.

Motor activity

Data generated during the study did not reveal any significant differences between control and treated animals. Females tended to be more active than males at the 1- and 3 month evaluation points, however there was no [sex x treatment] interaction and this finding was considered incidental.

Body temperature

There was a slight but significant decrease in body temperature in high dose animals at the end of the main phase of the study (0.6 degree C reduction in females, 0.3 degree C reduction in males).

Observations at necropsy

There were no gross changes observed at necropsy that were considered related to treatment with PDC. Absolute brain weight was decreased by approx. 10% in high dose animals, probably reflecting the lower body weight noted above.

Relative brain weight was marginally increased.

Histopathologic observations

A few incidental observations were identified however the incidence was similar in control and high dose animals, and the changes were considered unrelated to PDC treatment.

Recovery phase

Body weight decreases present in high dose males at the end of the main phase of the study were maintained throughout the 9 wk recovery phase (signifiant 8% decrease in high dose males at wk 22). Mid dose males and high dose females showed a non-significant 3-4% reduction in bwt over the same period.

Body temperature differences in high dose animals generally remained during the recovery period (significantly decreased by 0.6 - 1.0 degree C in females throughout recovery phase, 0.3-0.5 degree C reduction in males during wk 1-4 only).

No gross lesions were identified at necropsy.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion : Under the conditions of the study, early transient

: Under the conditions of the study, early transient clinical signs and minor decreases in body weight and body temperature were the only effects attributable to PDC. A NOAEL of 20 mg/kg bwt/d was established in males (reflecting bwt effects only) and a NOAEL of 65 mg/kg bwt in females. The NOAEL for gross, microscopic and functional effects on the central and peripheral nervous system was 200 mg/kg (the

highest does tested) bwt in both sexes.

Reliability : (1) valid without restriction

GLP guideline study.

Flag : Critical study for SIDS endpoint

25.10.2004 (216)

5.10 EXPOSURE EXPERIENCE

Type of experience : Human

Remark: An unconscious 71-year-old man was taken to the hospital

approximately 1 hour after attempting suicide by ingesting approximately 180 ml of a cleaning agent (labelled as 90 % 1,2-dichloropropane and 10 % 1,1,1-trichloroethane). He died after 48 hours never regaining consciousness. Upon arrival his liver and renal functions as well as coagulation were normal but 8 hours later, severe liver dysfunctions appeared. These dysfunctions were detected by a strong increase of transaminase activity in serum. After 48 hours aspartate aminotransferase activity was 5,912 U/I (upper normal value 19U/I), the alanine aminotransferase was 30,128 U/I (normal value 5-23 U/I) and prothrombin activity was lower than 10%. Further, the following were measured: a bilirubin content of 2.3 mg/100 ml (normal value < 1mg/100ml), a creatinine content of 2.8mg/100ml (normal value 0.7-1.1 mg/100 ml), an increased activity of

cholinesterase up to 2100 U/l, a fibrinogen content of 96 mg/100 ml (normal value 150-450 mg/100 ml) and 14000 blood

platelets/ul. During the hospital stay, the patient was

diagnosed with severe liver and renal dysfunction, abnormal coagulation (coagulopathy), metabolic acidosis, myocardial

insufficiency and shock.

Estimated dose (180mL of 90% PDC) is 3400 mg/kg/day for a 60kg 71-

year old.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (2) valid with restrictions

Short case report, limited reporting of methods and results. Includes an

approximate dose and some available toxicological data.

20.10.2004 (217) (218)

Type of experience : Human

Remark: A 20-year-old girl was taken to a hospital with vomiting and

abdominal pains. During the examination oliguria, epistaxis, hematocyturia, metrorrhagia as well as periorbital and conjunctival hemorrhages were found. The clinicochemical examination showed acute liver disease (increased activities of alanine and aspartate aminotransferase as well as an increased bilirubinemia and a decreased prothrombin level), severe kidney disease (hypercreatininemia and decreased urea

value), hemolytic anemia and intravascular coagulation

(increased fibrinolytic split products; number of

thrombocytes 10,000/mm3). Further, complement factors C3 and

C4 were not detectable. Three weeks after a blood transfusion and a hemofiltration, the liver, kidney and

coagulation dysfunction were no longer detectable. Review of the patient's medical history presumed a connection between appearance of these symptoms and the abuse of "Trielina". The

patient was sniffing "Trielina" for approximately 1 month, stopped for 10 months and then started again - the

above-mentioned intoxication symptoms returned. The product contained 98% 1,2-dichloropropane and 2% trichloroethylene and dichloroethane

based on GC analysis.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Short case report, limited reporting of methods and results, unknown

reliability.

29.02.2004 (219)

Type of experience: Human

Remark: A unconscious 49-year-old man was taken to the hospital

after attempting suicide by ingesting an unknown amount of 1,2-

dichloropropane, as identified by GC/MS. The patient was given artificial respiration and regained consciousness 3 days later. He was diagnosed with esophagitis. The following biochemical parameters were

analyzed in serum at different times: alanine

aminotransferase activity and the bilirubin content were increased for the first 2 weeks but normalized within approximately 1 month; Three days after arrival the

prothrombin content severely decreased (20% of the starting

value) and 9 days later it returned to normal.

One month after intoxication, hepatomegaly and splenic

enlargement as well as ascites appeared. Liver

biopsy revealed hepatocellular necrosis accompanied by an

inflammatory reaction. Six months later another

biopsy was taken; portal hypertension and portal fibrosis

were found but there was no remaining evidence of hepatocyte necrosis.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable
Short case report, limited reporting of methods and results, unknown

reliability.

20.10.2004 (220)

Type of experience: Human

Remark: A 46-year old man fell in a deep coma with pupil dilation

and hypertension within 2 hours after ingesting approximately

50 ml of a cleaning agent by mistake; the man gained consciousness 24 hours after being given artificial respiration and osmotic diuresis. A little bit later

delirium and tremor appeared. The man died 36 hours after intake, of irreversible shock with heart failure, acidosis

and hepatic

cytolysis. Autopsy showed a centrilobular and mediolobular

acute necrosis of the liver. Gas chromatography analysis of the cleaning agent demonstrated qualitatively the presence of 1,2-dichloropropane.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown

reliability.

20.10.2004 (221)

Type of experience : Human

Remark: In a letter to the editor, a case report is described for a

73 yr old woman who was admitted to hospital with vomitting and somnolence. Three days earlier she had developed abdominal pains. The patient had been cleaning gar ments

using a stain remover containing 1,2-dichloropropane (no analytical

confirmation of composition). She reported

having fallen asleep for 2 hr with her head about 40 cm away from the

open glass of cleaning fluid.

Laboratory tests revealed decreased serum potassium, hyperglycemia and leukocytosis. Serum ASAT increased from 2114 U/I on the day of admission to 6300 U/I the following day, and serum ALAT from 1990 U/I to 5400 U/I; prothrombin

activity decreased from 31% of normal to 22% of normal over the same

period.

Her condition had improved by day 5 (no details).

Hepatic biopsy on day 8 revealed centrilobular necrosis, characterised by pyknosis and 'cellular shadows'.

Haemolytic anaemia (Hb 9.8 g/l; 3.01 x 10^6 ul red cells; HCT 30%) was present at day 10 and persisted for 10 days.

After 3 weeks, haematologic parameters were normal.

After 6 months, ASAT and ALAT were slightly elevated (55 and

75 U/I, respectively).

All tests were normal by 9 months.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown

reliability.

29.02.2004 (222)

Type of experience : Human

Remark: In a letter to the editor, the authors report a 46 yr old

individual who was admitted to hospital with symptomatic wide-complex tachiarrythmia, with subsequent diagnosis of hyperkalemia and oliguric acute renal failure and symptoms of hepatocellular necrosis, rhabdomyolysis, and a severe

coagulopathy.

Symptoms were reported shortly after having worked for 6 hours in an outdoor environment with a commercial paint

fixative reported to contain 35-40% 1,2-dichloropropane and toluene (33-

38%). An accidental spill resulted in gross

contamination of the front part of his body, trunk and

abdomen. The individual delayed removal of his clothes and skin decontamination for 5 hours suggesting probable massive dermal exposure with prolonged inhalation exposure also likely. He

reported only transient redness of the involved skin areas.

The patient responded favorably to treatment and became non-oliguric after two 10-hr sessions of dialysis over 2 d while coagulation values returned to normal over the same period. The patient was discharged after 7 d. Full renal and hepatic function recovery was demonstrated after 2 weeks.

The authors summarize that this case represents a severe acute intoxication from 1,2-PDC via a percutaneous route of exposure, but acknowledge that additional mechanisms, which may

have played a contributing role, could not be excluded.

Reviewer's Comment:

Although the authors state that exposure is via dermal contact, given the high volatility of PDC, it is likely that inhalation of volatilized material was a major contributor to exposure during the 5-hour period while he was

wearing his "drenched" shirt.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown

reliability.

25.10.2004 (223)

5.11 ADDITIONAL REMARKS

Type : Biochemical or cellular interactions

Remark: Inhalational exposure of 1,2-dichloropropane in

concentration 10 mg/m3 for 3 months induced an increased

lipid content in the cells of the adrenal gland cortex.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (224)

Type: Biochemical or cellular interactions

Remark : Test condition:

[14C]-marked 1,2-dichloropropane was dosed to female F344 rats via oral gavage in concentrations of 0.94; 7 and 255

mg/kg.

Results:

Radiolabel was exhaled as CO2 in concentration 27; 17 and 2 %. The liver was taken from the animals six hours after the application.

Radioactivity measurement was 83 dpm/mg in the low dose group, 470 dpm/mg in the middle dose group and 52 dpm/mg in the high dose group.

90 - $95\ \%$ of this radioactivity was analyzed in the isolated liver-DNA.

After the "acid depurinisation" of DNA, it was found that radioactive precursors of the nucleotide were present at biosynthesis and not during the covalent binding of radioactive 1,2-dichloropropane on DNA.

Maximal DNA-damage, given as the covalent binding index (CBI = mmol of substance bound per mol nucleotide/mmol substance applied per kg body weight), was < 2 for the low dose group, < 1 for the middle dose group and < 0.3 for the high dose group.

It can be assumed there is no strong (if existing) genotoxic risk in-vivo for 1,2-dichloropropane, as a large database already exists.

Source Reliability

Source

Reliability

: The 1,2-Dichloropropane ICCA/HPV Consortium

: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (225)

Type : Biochemical or cellular interactions

Remark : Test condition:

Two female F344 rats were inhalational exposed to radioactive [14C]-1,2-dichloropropane resulting in intake of 25 and 27 mg/kg.

Results:

The substance was exhaled for 7 and 7.5 hours as 18 % and 14 % CO2. At the end of the test, the animal livers were taken and DNA was isolated. Specific radioactivity in DNA was 350 dpm/mg. The separation of the DNA in natural nucleotides showed that the radioactivity is caused when the precursors were added to DNA during biosynthesis. The DNA-adducts can only be less than 3.1 % of the radioactivity in DNA. The covalent binding index CBI was given as < 0.7. This maximum possible CBI classifies 1,2-dichloropropane as 10000 times below the genotoxic potential of aflatoxin B1. A binding on DNA as an important mechanism of carcinogenic effect of

1,2-dichloropropane is improbable.
The 1,2-Dichloropropane ICCA/HPV Consortium

: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (226)

Type : Cytotoxicity

Remark: Rats and mice were exposed to 10 mg 1,2-dichloropropane/m3.

Pulmonary arteries, veins and capillaries were

histologically analyzed at different times. Vacuolization of endothelia cells and invagination of the karyolemma in the

ld 78-87-5 5. Toxicity Date 14.12.2004

> nucleus appeared after 5 days. Pinocytic rate was increased in cytoplasm of the endothelial cells after 13 days. Bladders between the capillaries were built after 50 days and a destruction of mitochondria and organelles followed. NADH dehyrogenase and glucose-6-phosphate dehydrogenase activity was significantly (p < 0.01) increased and after 15 and 30 days these activities returned to the control group

Source The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (227)

Type Cytotoxicity

Remark An increase of conglomeration in cytoplasm of fat cells as

well as an increase of vacuolization and degranulation was

caused after 7 days exposure to 1000 mg

1,2-dichloropropane/m3. An increase of functional activity

of fat tissue cells was also found.

The 1,2-Dichloropropane ICCA/HPV Consortium Source

Reliability (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (228)

Type Cytotoxicity

Remark Method:

> In this study we have investigated the effects of DCP on intracellular glutathione (GSH) content in main target tissues of male Wistar rats, i.e. liver, kidney and blood, in order to establish if a correlation between DCP-induced

GSH depletion and tissue damage exists.

Results:

Administration of DCP (2 ml/kg body weight, orally) caused a dramatic loss of tissue GSH occurring 24 h after DCP intoxication, followed by a slow restoration approaching physiological levels after 96 h. GSH depletion was associated with a marked increase in serum GOT, GPT, 5'-nucleotidase, gamma-glutamyl transpeptidase, alkaline phosphatase, urea and creatinine, and a significant decrease

of hemolysis.

When animals were pretreated with a GSH depleting agent, buthionine-sulfoximine (BSO; 0.5 mg/kg body weight; i.p.) 4 hours before DCP intoxication, an increase of overall mortality was found, significantly different from the group of animals treated only with DCP. On the contrary, the administration of a GSH precursor, N-acetylcysteine (NAC) i.p. (250 mg/kg b.w.) 2 and 16 hours after DCP intoxication prevented the dramatic loss of cellular GSH and reduced the extent of injury in target tissues, as demonstrated by laboratory indices. Furthermore, statistical analysis of the data revealed a correlation between:

- 1) depletion of liver GSH and increase in serum GOT, GPT, 5'-nucleotidase
- 2) depletion of kidney GSH and increase in serum urea and creatinine and
- 3) depletion of blood GSH and the occurrence of hemolysis.

The findings demonstrate that GSH plays a critical role in modulating the toxicity of DCP. They also highlight the protective role of NAC and suggest that this glutathione precursor could rationally be used in DCP poisoning in

humans.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (229)

Type : Distribution

Remark: Ninety-six hours after the administration of 0.88 mg

[14C]1,2-dichloropropane/animal, Carworth Farm rats (6 animals/sex) were dissected and 0.5 % of the radioactivity was still present in the intestinal tract, 1.7 %(male) and 1.4 % (female) in the skin and 4.1 % (male) and 3.2 %

(female) in the remainder of the body.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (230)

Type : Distribution

Remark : Partition coefficients for 1,2-dichloropropane were

analyzed in vitro at 37 degrees C and resulted in:

blood (rat)/air 18.5 +- 0.5

blood (human being)/air 10.7 + 0.5blood (human being)/air 8.75 + 0.50

fat tissue/air 499 +- 30 liver tissue/air 24.8 +- 2.4 muscle tissue/air 12.0 +- 1.1

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (120) (121)

Type : Excretion

Remark: Ninety-six hours after the administration of 0.88 mg

[14C]1,2-dichloropropane/animal, Carworth Farm rats (6 animals/sex) were dissected and 51.1 % (male) and 54.4 % (female) of the radioactivity eliminated with urination, 6.8 % (male) and 4.9 % (female) was eliminated with faeces.

After

administering the above-mentioned dosage to females (n = 5), within 96 hours, the exhalation was 19.3 % of radioactivity in the form of CO2 and 23.1 % as non-identified evaporable

substances.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (230)

Type : Excretion

Remark: Urine and feces of F344 rats (4 animals/sex/concentration)

were collected for 48 hours after inhalational exposure

(head only) for 6 hours to 24, 235 and 470 mg

[14C]1,2-dichloropropane/m3. 55 - 65 % of the recovered radioactivity was detected in urine and 6.3 - 9.7 % was detected in feces; 16 - 23 % of the radioactivity was

exhaled as CO2.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (231)

Type : Metabolism

Remark: The main metabolites of 1,2-dichloropropane were identified

in urine of Sprague-Dawley and F344 rats. Metabolites were

N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine and

N-acetyl-S-(1-carboxyethyl)-L-cysteine. A quantitative analysis showed that approximately 25 - 30 % of a single oral administration of 100 mg 1,2-dichloropropane/kg body weight was conjugated with glutathione in Sprague-Dawley

rats

which produced mercapture acid derivative

N-acetyl-S-(2-hydroxypropyl)-L-cysteine. The urine of F344 rats was analyzed after the administration of 100 mg /kg body weight and 10.2 % of the administered dose was recovered as N-acetyl-S-(2-hydroxypropyl)-L-cysteine, 14.5 %

as N-acetyl-S-(2-oxopropyl)-L-cysteine and 1.8 % as N-acetyl-S-(1-carboxyethyl)-L-cysteine was found. The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (232) (233) (231)

Type : Metabolism

Source

Remark: During the oxidation of 1,2-dichloropropane (either before

or after the conjugaton with glutathione), the buildup of

N-acetyl-S-(1-carboxyethyl)-L-cysteine and

N-acetyl-S-(2-oxopropyl)-L-cysteine appeared. The later

product can be further reduced to

N-acetyl-S-(2-hydroxypropyl)-L-cysteine. The process of 1,2-dichloropropane oxidation to lactate creates CO2 and acetyl-CoA accumulation, which is either exhaled or enters

the citric acid cycle, respectively. It is shown that

1,2-dichloropropane can also be exhaled unchanged. 61 - 87 %

of the exhaled radioactivity was identified as

1,2-dichloropropane, independent of administration route (inhalational or orally). Sex and administration route had

no effect on the metabolism.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (231)

Type : other: Biotransformation

Remark: Analysis with rat liver microsomes showed that the enzyme

responsible for the dechlorination of 1,2-dichloropropane

needs O2 and NADPH. Phenobarbital and benzpyrene can induce

this enzyme but not methylcholanthrene.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (234)

Type : other: Biotransformation

Remark: Various in vitro tests for oxidation of 1,2-dichlororpopane

in human liver microsomes showed that during this oxidation the most important enzyme probably is P-450 II E1 isozyme.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine

reliability.

26.10.2004 (235)

Type : other: Resorption

Remark: The highest levels of 1,2-dichloropropane in blood were

detected 30 -60 minutes after the administration of 55 - 440 mg 1,2-dichloropropane/kg body weight in male Wistar rats (5 animals/dose group). The half-life of 1,2-dichloropropane in blood was 3.1 - 5.0 hours after the administration of 55 - 220 mg/kg. After the administration of 440 mg/kg, the maximal blood level was reached after only 2 hours. The half-life for 1,2-dichloropropane in blood was then 13.6

hours.

Source : The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability : (4) not assignable

26.10.2004 (217)

Remark: In addition to N -acetyl -S-(2-hydroxypropyl)cysteine, in the

study on metabolism of 1,2-dichloropropane, two other metabolites were found in urine of Sprague-Dawley rats. They were identified as N-acetyl-S-(2,3-dihydroxypropyl)cysteine and beta-chlorolacate. The presumption would be that

metabolism of 1,2-dichloropropane to

N-acetyl-S-(2-hydroxypropyl)cysteine follows a

dechlorination and oxidation step to

1-chloro-2-hydroxypropane. Further dechlorination produces N-acetyl-S-(2-hydroxypropyl)cysteine. Analysis of urine showed two substances beta -chlorolactate and

S-(2,3-dihydroxypropyl)cysteine, which could have originated

from 1-chloro-2-hydroxypropane.

Source : Dow Europe

DOW Europe Horgen A.K. Mallett Surrey

25.10.2004 (233)

6. Analyt. Meth. for Detection and Identification

ld 78-87-5 **Date** 14.12.2004

- 6.1 ANALYTICAL METHODS
- 6.2 DETECTION AND IDENTIFICATION

7. Eff. Against Target Org. and Intended Uses

ld 78-87-5 **Date** 14.12.2004

7.1	FUNCTION
7.2	EFFECTS ON ORGANISMS TO BE CONTROLLED
7.3	ORGANISMS TO BE PROTECTED
7.4	USER
1.7	OCEN
	77071107
7.5	RESISTANCE

8. Meas. Nec. to Prot. Man, Animals, Environment

ld 78-87-5 **Date** 14.12.2004

8.1	METHODS HANDLING AND STORING
8.2	FIRE GUIDANCE
8.3	EMERGENCY MEASURES
8.4	POSSIB, OF RENDERING SUBST, HARMLESS
-	
8.5	WASTE MANAGEMENT
0.10	
8.6	SIDE-EFFECTS DETECTION
0.0	GDE ET EGIO DETEGNON
8.7	SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER
0.7	SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER
88	REACTIVITY TOWARDS CONTAINER MATERIAL
XX	REALTIVITY TOWARDS CONTAINER WATERIAL

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10. Summary and Evaluation

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10.1 END	POINT S	SUMMARY
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10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT